Clinical Policy: Omalizumab (Xolair)
Reference Number: CP.PHAR.01
Effective Date: 10/08
Last Review Date: 02/17

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for omalizumab (Xolair®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that omalizumab is medically necessary when one of the following criteria are met:

I. Initial Approval Criteria
   A. Moderate to Severe Persistent Asthma (must meet all):
      1. Prescribed by a pulmonologist or allergist;
      2. Diagnosis of moderate to severe persistent asthma;
      3. Age ≥ 6 years;
      4. Member who smokes is engaged in smoking cessation efforts;
      5. Member has experienced at least TWO exacerbations requiring oral/systemic corticosteroids treatment, urgent care visit, or hospital admission within the last 12 months, despite adherent use of controller therapy (i.e., combination of a high-dose inhaled corticosteroid [ICS] plus a long acting beta-2 agonist [LABA] or a high-dose ICS plus a leukotriene modifier [LTRA] if LABAs are contraindicated or member is intolerant);
      6. Xolair is prescribed concomitantly with a combination of inhaled corticosteroids plus long-acting beta-2 agonists and/or leukotriene modifiers;
      7. IgE level between 30-1300 IU/mL;
      8. History of FEV₁ baseline < 80% of predicted;
      9. Positive immunoassay or skin test to perennial aeroallergen identified to be a trigger for the patient’s asthma;
      10. Prescribed dose does not exceed 375 mg administered every 2 weeks, and is appropriate, based upon pre-treatment IgE level and current weight per Appendix B.

   Approval duration: 3 months

   B. Chronic Idiopathic Urticaria (must meet all):
      1. Age ≥ 12 years;
      2. Prescribed by a dermatologist or allergist;
      3. Diagnosis of chronic idiopathic urticaria (CIU);
      4. Failure of or intolerance to both of the following steps:
         a. Step 1: use of 2 antihistamines (at least one must be a second generation – e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine, ranitidine,
famotidine, cimetidine) at maximum indicated doses, unless contraindicated, each for at least 4 weeks;
   b. Step 2: use of a leukotriene receptor antagonist concurrently with an antihistamine at maximum indicated dose for at least 4 weeks;
4. Prescribed dose does not exceed 300mg every 4 weeks.

Approval duration: 3 months

C. **Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.

II. **Continued Approval**
   A. **Moderate to Severe Persistent Asthma:**
      1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
      2. Member is adherent to controller therapy with a combination of inhaled corticosteroids plus long-acting beta-2 agonists and/or leukotriene modifiers;
      3. Documentation supports positive response to therapy.

      Approval duration: 6 months

   B. **Chronic Idiopathic Urticaria:**
      1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
      2. Documentation supports positive response to therapy;
      3. Prescribed dose does not exceed 300mg every 4 weeks.

      Approval duration: 6 months

   C. **Other diagnoses/indications** (must meet 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
      2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

*Description/Mechanism of Action:*
Xolair is a recombinant DNA-derived humanized IgG1κ monoclonal antibody that selectively binds to human immunoglobulin E (IgE).

*Asthma:* Omalizumab inhibits the binding of IgE to the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils. Reduction in surface-bound IgE on FcεRI-bearing cells limits the degree of release of mediators of the allergic response. Treatment with Xolair also reduces the number of FcεRI receptors on basophils in atopic patients.
**Clinical Policy**

**Omalizumab**

*Chronic Idiopathic Urticaria:* Omalizumab binds to IgE and lowers free IgE levels. Subsequently, IgE receptors (FcεRI) on cells down-regulate. The mechanism by which these effects of omalizumab result in an improvement of CIU symptoms is unknown.

**FDA Approved Indication(s):**

Xolair is a monoclonal antibody/subcutaneous injection indicated for:

- **Moderate to severe persistent asthma**
  - Patients 6 years of age and older 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.
- **Chronic idiopathic urticaria**
  - The treatment of adults and adolescents (12 years of age and above) with chronic idiopathic urticaria who remain symptomatic despite H1 antihistamine treatment.

**Limitations of use:**

- Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus;
- Xolair is not indicated for treatment of other allergic conditions;
- Xolair is not indicated for treatment of other forms of urticaria.

**Safety Information:**

Warning- anaphylaxis: Anaphylaxis presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair. Anaphylaxis has occurred as early as after the first dose of Xolair, but also has occurred beyond 1 year after beginning regularly administered treatment. Because of the risk of anaphylaxis, observe patients closely for an appropriate period of time after Xolair administration. Health care providers administering Xolair should be prepared to manage anaphylaxis that can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur.

**Appendices**

**Appendix A: Abbreviation Key**

CIU: chronic idiopathic urticarial  
FEV: forced expiratory volume  
IgE: immunoglobulin E  
IgG: immunoglobulin G

**Appendix B:**

**Recommended Dose for Asthma Based on Pre-treatment IgE and Body-weight, Ages 12 and older:**

- **IgE 30—100 International Units/mL**
  
  91—150 kg = 300 mg subcutaneously every 4 weeks.
  30—90 kg = 150 mg subcutaneously every 4 weeks.
**IgE 101—200 units/mL**
91—150 kg = 225 mg subcutaneously every 2 weeks.
30—90 kg = 300 mg subcutaneously every 4 weeks.

**IgE 201—300 units/mL**
91—150 kg = 300 mg subcutaneously every 2 weeks.
61—90 kg = 225 mg subcutaneously every 2 weeks.
30—60 kg = 300 mg subcutaneously every 4 weeks.

**IgE 301—400 units/mL**
> 90 kg = No dosage recommendations are available; the manufacturer does not recommend use in this population.
71—90 kg = 300 mg subcutaneously every 2 weeks.
30—70 kg = 225 mg subcutaneously every 2 weeks.

**IgE 401—500 units/mL**
> 90 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.
71—90 kg = 375 mg subcutaneously every 2 weeks.
30—70 kg = 300 mg subcutaneously every 2 weeks.

**IgE 501—600 units/mL**
> 70 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.
61—70 kg = 375 mg subcutaneously every 2 weeks.
30—60 kg = 300 mg subcutaneously every 2 weeks.

**IgE 601—700 units/mL**
> 60 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.
30—60 kg = 375 mg subcutaneously every 2 weeks.

**Recommended Dose for Asthma Based on Pre-treatment IgE and Body-weight, Ages 6 to < 12 years:**

**IgE 30—100 International Units/mL**
20—40 kg = 75 mg subcutaneously every 4 weeks.
41—90 kg = 150 mg subcutaneously every 4 weeks.
91—150 kg = 300 mg subcutaneously every 4 weeks.

**IgE 101—200 units/mL**
20—40 kg = 150 mg subcutaneously every 4 weeks.
41—90 kg = 300 mg subcutaneously every 4 weeks.
91—125 kg = 225 mg subcutaneously every 2 weeks.
126—150 kg = 300 mg subcutaneously every 2 weeks.
**IgE 201—300 units/mL**
20—30 kg = 150 mg subcutaneously every 4 weeks.
31—40 kg = 225 mg subcutaneously every 4 weeks.
41—60 kg = 300 mg subcutaneously every 4 weeks.
61—90 kg = 225 mg subcutaneously every 2 weeks.
91—125 kg = 300 mg subcutaneously every 2 weeks.
126—150 kg = 375 mg subcutaneously every 2 weeks.

**IgE 301—400 units/mL**
20—30 kg = 225 mg subcutaneously every 4 weeks.
31—40 kg = 300 mg subcutaneously every 4 weeks.
41—70 kg = 225 mg subcutaneously every 2 weeks.
71—90 kg = 300 mg subcutaneously every 2 weeks.
> 90 kg = No dosage recommendations are available; the manufacturer does not recommend use in this population.

**IgE 401—500 units/mL**
20—25 kg: 225 mg subcutaneously every 4 weeks.
26—31 kg: 300 mg subcutaneously every 4 weeks.
31—50 kg: 225 mg subcutaneously every 2 weeks.
51—70 kg: 300 mg subcutaneously every 2 weeks.
71—90 kg: 375 mg subcutaneously every 2 weeks.
> 90 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

**IgE 501—600 units/mL**
20—30 kg: 300 mg subcutaneously every 4 weeks.
31—40 kg: 225 mg subcutaneously every 2 weeks.
41—60 kg: 300 mg subcutaneously every 2 weeks.
61—70 kg: 375 mg subcutaneously every 2 weeks.
> 70 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

**IgE 601—700 units/mL**
20—25 kg: 300 mg subcutaneously every 4 weeks.
26—40 kg: 225 mg subcutaneously every 2 weeks.
41—50 kg: 300 mg subcutaneously every 2 weeks.
51—60 kg: 375 mg subcutaneously every 2 weeks.
> 60 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

**IgE 701—800 units/mL**
20—30 kg: 225 mg subcutaneously every 2 weeks.
31—40 kg: 300 mg subcutaneously every 2 weeks.
41—50 kg: 375 mg subcutaneously every 2 weeks.
CLINICAL POLICY
Omalizumab

> 50 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

- **IgE 801—900 units/mL**
  - 20—30 kg: 225 mg subcutaneously every 2 weeks.
  - 31—40 kg: 300 mg subcutaneously every 2 weeks.
  - 41—50 kg: 375 mg subcutaneously every 2 weeks.
  - > 50 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

- **IgE 901—1000 units/mL**
  - 20—25 kg: 225 mg subcutaneously every 2 weeks.
  - 26—30 kg: 300 mg subcutaneously every 2 weeks.
  - 31—40 kg: 375 mg subcutaneously every 2 weeks.
  - > 40 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

- **IgE 1001—1100 units/mL**
  - 20—25 kg: 225 mg subcutaneously every 2 weeks.
  - 26—30 kg: 300 mg subcutaneously every 2 weeks.
  - > 30 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

- **IgE 1101—1200 units/mL**
  - 20—25 kg: 300 mg subcutaneously every 2 weeks.
  - > 30 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

- **IgE 1201—1300 units/mL**
  - 20—25 kg: 300 mg subcutaneously every 2 weeks.
  - 26—30 kg: 375 mg subcutaneously every 2 weeks.
  - > 30 kg: No dosage recommendations are available; the manufacturer does not recommend use in this population.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J2357</td>
<td>Injection, omalizumab, 5 mg</td>
</tr>
<tr>
<td>Reviews, Revisions, and Approvals</td>
<td>Date</td>
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<tr>
<td>--------------------------------------------------------------------------------------------------</td>
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<tr>
<td>References updated. Removed “Available Dosing” section.</td>
<td>08/10</td>
</tr>
<tr>
<td>Converting to Caremark SGM criteria for Xolair.</td>
<td>09/11</td>
</tr>
<tr>
<td>Changed baseline serum IgE level from ≥30 to ≥30 IU/mL</td>
<td>10/12</td>
</tr>
<tr>
<td>Converted to Centene policy template</td>
<td>08/13</td>
</tr>
<tr>
<td>Added questions regarding dosing to algorithms and Appendix C dosing tables</td>
<td>12/13</td>
</tr>
<tr>
<td>Removed peak flow meter reading improvement from reauthorization algorithm</td>
<td>02/14</td>
</tr>
<tr>
<td>Added indication for urticaria</td>
<td>06/14</td>
</tr>
<tr>
<td>Reworded FDA-approved indication to mirror package insert.</td>
<td>04/15</td>
</tr>
<tr>
<td>Appendix B: Modified appendix to require use of high-dose corticosteroids along with leukotriene modifiers, rather than leukotriene modifiers by themselves.</td>
<td></td>
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<tr>
<td>Figure 1: Modified wording to read “Does patient practice adequate ICS dose titration or use of oral steroid therapy for asthma exacerbations?”</td>
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<tr>
<td>Figure 3: Modified algorithm to require failure or intolerance to at least two (rather than one) H1 antihistamines at maximum tolerated doses.</td>
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<tr>
<td>Policy converted to new format.</td>
<td>3/16</td>
</tr>
<tr>
<td>Age included per PI; all documentation requests removed; modified requirement for 3 months of adherent use to requirement for at least 2 exacerbations in the last 12 months despite adherent use of controller medication; changed “RAST” to “immunoassay.” Changed requirement for nonsmoker and nonsmoking home to engaged in smoking cessation efforts if smoker. Added requirement for concomitant use of maintenance therapy in asthma. Added failure or contraindication to step therapy for CIU. Removed criteria regarding response to therapy and rescuer inhaler use from asthma renewal criteria; removed questions about adverse reaction to Xolair for continuation of therapy requirement for both asthma and CIU; added maximum allowed dose to asthma and CIU criteria; added “positive response” to CIU continuation criteria; added definition of positive response to asthma continuation criteria; added safety information to background regarding anaphylaxis and provider administration of Xolair.</td>
<td></td>
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<tr>
<td>Minimum age changed to 6 for asthma, per PI. Added pediatric dosing to Appendix B.</td>
<td>9/16</td>
</tr>
<tr>
<td>Asthma step therapy edited to require LABAs before LTRAs unless contraindicated or intolerant.</td>
<td>02/17</td>
</tr>
<tr>
<td>CIU: Examples of second-generation antihistamines added.</td>
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<tr>
<td>Initial criteria: IgE level between 30-700 IU/mL is edited to read “between 30-1300 IU/mL” per PI.</td>
<td>03/17</td>
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References

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional...
medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.

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