Medical Policy

BlueCross BlueShield of Kansas
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Title: Xolair® (omalizumab)

- **Prime Therapeutics will review Prior Authorization requests.**
  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-1304KS-XOLA.pdf

  Link to Drug List (Formulary):
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional
Original Effective Date: August 2003
Revision Date(s): April 15, 2005; May 24, 2006; December 1, 2011; April 2, 2012; June 7, 2013; October 4, 2013; August 15, 2014, June 1, 2015; April 15, 2016; January 1, 2017; May 15, 2017; May 1, 2018; November 1, 2018; December 3, 2018
Current Effective Date: December 3, 2018

Institutional
Original Effective Date: October 6, 2008
Revision Date(s): December 1, 2011; April 2, 2012; June 7, 2013; October 4, 2013; August 15, 2014; June 1, 2015; April 15, 2016; January 1, 2017; May 15, 2017; May 1, 2018; November 1, 2018; December 3, 2018
Current Effective Date: December 3, 2018

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DESCRIPTION

The intent of the Xolair (omalizumab) Prior Authorization (PA) Criteria is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies while adhering to the dosing guidelines for age, weight, and pretreatment

IgE levels (for allergic asthma) as recommended in FDA labeling. For renewal of therapy, all dosing parameters must continue to be met with omalizumab contributing to the improvement or maintenance of asthma or improvement of urticaria symptoms.

Target Agent

- **Xolair**® (omalizumab)

FDA Approved Indications and Dosage[1]

Agent	Indications* ^	Dose and administration
Xolair® (omalizumab) subcutaneous injection	Moderate to severe persistent asthma in 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	75 mg to 375 mg by subcutaneous injection every 2-4 weeks. Determine the dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg)
	Chronic idiopathic urticarial in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment	Administer 150 or 300 mg by subcutaneous injection every 4 weeks

* Omalizumab is not indicated for treatment of other allergic conditions, other forms of urticaria, relief of acute bronchospasms, or status asthmaticus.
^ Omalizumab has not been studied for use in combination with Cinqair (reslizumab) or Nucala (mepolizumab).

POLICY

Prior Authorization Criteria for Approval

Initial Evaluation

Xolair (omalizumab) will be approved when **ALL** of the following are met:

1. ONE of the following:
   A. The patient has a diagnosis of moderate to severe persistent asthma, AND **ALL** of the following:
      i. If the patient is 6 to less than 12 years of age, the patient meets BOTH of the following:
         a. The pretreatment IgE level is 30 IU/mL to 1300 IU/mL
            AND
         b. The patient's weight is 20 kg to 150
         AND
      ii. If the patient is 12 years of age and over, the patient meets ALL of the following:
         a. The pretreatment IgE level is 30 IU/mL to 700 IU/mL
            AND
         b. The patient's weight provided for review of dose) is 30 kg to 150 kg
            AND
         c. The patient has a baseline FEV_1 <80% predicted
         AND

iii. Allergic asthma has been confirmed by a positive skin test or in vitro reactivity test (RAST) to a perennial aeroallergen
AND

iv. The patient has ONE of the following:
   a. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months
   OR
   b. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months
   OR
   c. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered

AND

v. ONE of the following:
   a. The patient is NOT currently being treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid in the past 90 days
   OR
   b. The patient is currently being treated with the requested agent AND is currently treated with an inhaled corticosteroid that is dosed as needed to control symptoms
   OR
   c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to inhaled corticosteroids

AND

vi. ONE of the following:
   a. The patient is currently treated with ONE of the following in the past 90 days:
      1) A long-acting beta-2-agonist (LABA)
      OR
      2) A Leukotriene receptor antagonist (LRTA)
      OR
      3) Long-acting muscarinic antagonist (LAMA)
      OR
      4) Theophylline

   OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to long-acting beta 2-agonists (LABA), leukotriene receptor antagonist (LRTA), Long-acting muscarinic antagonist (LAMA), AND theophylline

AND

vii. The requested dose is within dosing based on pre-treatment serum IgE level and the patient's body weight as defined in FDA approved labeling AND does NOT exceed 375 mg every 2 weeks

OR

B. The patient has a diagnosis of chronic idiopathic urticaria with at least 6 weeks of hives and itching AND **ALL** of the following:
   i. The patient is 12 years of age or over
   AND
   ii. ONE of the following:
      a. The patient has tried and had an inadequate response to TWO different classes of CIU therapies for at least 2 weeks duration of each course (first generation H-1 antihistamine [doxepin, hydroxyzine, cyproheptadine], second generation H-1 antihistamine [cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine], H-2 antihistamine [ranitidine, famotidine, cimetidine], leukotriene receptor antagonist [montelukast, zafirlukast])
      OR
      b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL prerequisite agents
   AND
   v. The requested dose is within the FDA labeled dose AND does NOT exceed 300 mg every 4 weeks

OR

C. The patient has another FDA approved indication, for the requested agent AND the requested dose is within the FDA labeled dose for the requested indication

AND

2. The prescriber is a specialist (e.g. allergist, immunologist, pulmonologist) in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

3. The requested agent will NOT be used in combination with an injectable IL-5 inhibitor (e.g. Cinqair, Fasenra, Nucala) for the requested indication

AND

4. The patient does NOT have any FDA labeled contraindication(s) to the requested agent

Length of Approval: 24 weeks for asthma and chronic idiopathic urticaria
12 months for all other FDA approved indications

Renewal Evaluation

Xolair (omalizumab) will be approved when **ALL** of the following are met:

1. The patient has been previously approved for the requested agent through the PA process
   AND
2. ONE of the following:
   A. The patient has a diagnosis of moderate to severe persistent asthma, AND **ALL** of the following:
      i. The patient's weight is within the FDA indicated range for their age (i.e. 20 kg to 150 kg for patients age 6 to less than 12 years and 30 kg to 150 kg (for patients 12 years of age and above)
      AND
      ii. The patient has had clinical response or disease stabilization as defined by ONE of the following:
         a. Increase in percent predicted FEV_1 from baseline
         OR
         b. Decrease in the dose of inhaled corticosteroid required to control the patient's asthma
         OR
         c. Decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma
         OR
         d. Decrease in the number of hospitalizations, need for mechanical ventilation, or visits to the emergency room or urgent care due to exacerbations of asthma
      AND
      iii. ONE of the following:
         a. The patient is currently treated and is compliant with standard therapy (e.g. inhaled corticosteroids, long acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), Long-acting muscarinic antagonist (LAMA), theophylline) in the past 90 days
         OR
         b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL standard therapies
      AND
      iv. The requested dose is based-on pre-treatment serum IgE level and the patient's body weight as defined in FDA approved labeling AND does not exceed 375 mg every 2 weeks

   OR

   B. The patient has a diagnosis of ~~is~~ chronic idiopathic urticaria, AND ALL of the following:
      i. The patient has had improvement in symptoms (e.g. number of hives, size of hives, reduction in itching)
      AND

ii. The requested dose is within the FDA labeled dose AND does NOT exceed 300 mg every 4 weeks

OR

C. The patient has another FDA approved indication for the requested agent AND the requested dose is within the FDA labeled dose for the requested indication

AND

3. The prescriber is a specialist (e.g. allergist, immunologist, pulmonologist) in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

4. The requested agent will NOT be used in combination with an injectable IL-5 inhibitor (e.g. Cinqair, Fasenra, Nucala) for the requested indication

AND

5. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of Approval: 12 months

Agent (s)	Contraindication(s)
Xolair® (omalizumab)	Severe hypersensitivity reaction to Xolair or any ingredient of Xolair

FDA Approved Dosing for Patients Age 6 to less than 12 Years

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight									
		20-25 kg	>25-30 kg	>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)									
30-100	Every 4 weeks	75	75	75	150	150	150	150	150	300	300
>100-200		150	150	150	300	300	300	300	300	225	300
>200-300		150	150	225	300	300	225	225	225	300	375
>300-400		225	225	300	225	225	225	300	300	DO NOT DOSE	
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375	DO NOT DOSE			
>600-700		300	225	225	300	375	DO NOT DOSE				
>700-800	Every 2 weeks	225	225	300	375	DO NOT DOSE					
>800-900		225	225	300	375						
>900-1000		225	300	375	DO NOT DOSE						
>1000-1100		225	300	375							
>1100-1200		300	300	DO NOT DOSE							
>1200-1300		300	375								

FDA-Approved Dosing for Patients 12 years of Age and Above

Pre-treatment serum IgE (IU/mL)	Body weight (kg)			
	30-60	> 60-70	> 70-90	> 90-150
≥ 30-100	150 mg q 4 wks	150 mg q 4 wks	150 mg q 4 wks	300 mg q 4 wks
> 100-200	300 mg q 4 wks	300 mg q 4 wks	300 mg q 4 wks	225 mg q 2 wks
> 200-300	300 mg q 4 wks	225 mg q 2 wks	225 mg q 2 wks	300 mg q 2 wks
> 300-400	225 mg q 2 wks	225 mg q 2 wks	300 mg q 2 wks	
> 400-500	300 mg q 2 wks	300 mg q 2 wks	375 mg q 2 wks	
> 500-600	300 mg q 2 wks	375 mg q 2 wks		
> 600-700	375 mg q 2 wks			

RATIONALE

Asthma

Asthma is a chronic inflammatory disorder of the airways.[2,3] It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.[2] Symptoms of asthma include wheezing, coughing, recurrent difficulty breathing, shortness of breath, and chest tightness.[2,3] Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles.[2] The National Asthma Education and Prevention Program (NAEPP) Expert Panel guidelines recommend the use of detailed medical history, physical examination, and spirometry to make a diagnosis of asthma. In addition, differential diagnosis of asthma should be considered.

The patient's asthma can be considered to be well controlled when asthma symptoms are twice a week or less; the rescue bronchodilator medication is used twice a week or less; there is no nocturnal or early morning awaking due to asthma symptoms; there are no limitations of work, school, or exercise; and the Forced Expiratory Volume (FEV1) is normal or the patient's personal best.[6] Markers of asthma that is not adequately controlled in patients receiving therapy include limitation of normal activities, poor lung function with FEV1 of <80% predicted, at least 2 episodes per year of asthma exacerbations requiring oral systemic corticosteroids.[2] More frequent and intense exacerbations (e.g. requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control.[4]

The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma.[3] Long-term goals for asthma management are to achieve good control of symptoms, maintain normal activity level and to minimize the future risk of exacerbations, fixed airflow limitation and side-effects.[3]

Allergic asthma is triggered by inhalation of allergens.[6] IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with low dose ICS in combination with a LABA.[3] Severe asthma is defined as "asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming 'uncontrolled' or which remains uncontrolled despite this therapy.[4] Early initiation of low dose inhaled corticosteroid (ICS) in patients with asthma has led to greater improvement in lung function than if initiation of ICS after symptoms have been present for more than 2 to 4 years.[3]

GINA recommends as-needed relieve inhaler, short acting b-agonist (SABA) as Step 1. SABAs are highly effective for the quick relief of asthma symptoms. However, there is insufficient evidence for use of SABA alone for the treatment of asthma. SABA monotherapy for the treatment of asthma should be reserved for patients with occasional daytime symptoms (less than twice a month) of short duration with no night waking and with normal lung function. Step 2 is the recommendation of treatment with ICS. At low doses, ICS reduces asthma symptoms, increases lung function, improves quality of life, and reduces the risk of exacerbations and asthma-related hospitalizations or death. Leukotriene receptor antagonists (LTRA) are less effective than ICS. Step 3 involves one or two maintenance inhalers and an as-needed reliever. Combination low dose and long acting b-agonist (LABA) as maintenance treatment plus an as-needed SABA or low dose ICS with formoterol (budesonide or beclometasone) with a reliever treatment are options recommended. Step 4 involves 2 or more maintenance agents with an as-needed reliever. Combination low dose ICS with formoterol or medium dose ICS with LABA and an as-needed SABA are recommended options. Step 5 includes higher level care and/or add-on treatment. Depending on treatment options used in previous steps, long acting muscarinic antagonists (LAMA) such as tiotropium, omalizumab, or anti-interluekin-5 (mepolizumab and reslizumab) are additional pharmacologic options as add-on therapy.[3]

In patients with moderate-to-severe asthma, treatment with omalizumab (compared with placebo) can decrease the incidence of exacerbations and result in a significant reduction in the dose of inhaled or oral glucocorticoids required to control symptoms. Omalizumab has never been compared directly in a controlled clinical trial with other asthma therapies, such as inhaled glucocorticoids with long-acting beta-agonists, anti-leukotriene agents, or allergen immunotherapy. Independent of other therapies, in patients with atopic severe asthma, who have a serum IgE level of 30 to 700 IU/mL and documented sensitivity to a perennial allergen, the addition of omalizumab can be considered. The response to treatment with omalizumab is variable and difficult to predict, ranging from 30-50% in patients with moderate to severe asthma. A minimum of 12 weeks of treatment is needed to assess efficacy. There is usually little to no improvement in FEV_1 and airway hyperreactivity when omalizumab is added to pre-existing therapy.[7,8]

Moderate to Severe Allergic (IgE-mediated) Asthma

Allergic asthma is triggered by inhalation of allergens.[6] IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with low dose ICS in combination with a LABA.[3] Severe asthma is defined as "asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy."[4] Guidelines recommend use of omalizumab as add on therapy for patients who have failed to respond to standard therapy and have IgE-mediated allergic asthma.

Chronic Idiopathic Urticaria (CIU)

Chronic urticaria is defined by the presence of urticarial (hives) that has been continuously or intermittently present for more than 6 weeks. CIU involves cutaneous mast cell granulation.[9] The wheals usually last less than 24 hours with itching being the most common symptom. Diagnosis involves evaluation of labs including a complete blood count with differential, stool samples

(assessing for parasitic activity), erythrocyte sedimentation rate, antinuclear antibody, hepatitis B and C titers, serum cryoglobulin and complement assays, thyroid function testing, and Chronic Urticaria index.

Treatment goals for CIU involves symptom control and improvement in quality of life that is acceptable to the patient. Guidelines recommend a step wise approach to treating CIU.[9-11] Initial treatment with H-1 antihistamines at higher than standard doses has been shown to adequately control CIU symptoms in 60-70% of patients.[9] A second generation H-1 antihistamine (cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine), dosed daily rather than as needed basis, is recommended as part of initial therapy.[10,11] If there is insufficient response, the second step is to implement one or more of the following strategies:

- Addition of a different second generation H-1 antihistamine
- Addition of a first-generation H-1 antihistamine at nighttime (doxepin, hydroxyzine, cyproheptadine)
- Addition of H-2 antihistamine (ranitidine, famotidine, cimetidine)
- Addition of leukotriene receptor antagonist (montelukast, zafirlukast), especially in patients with NSAID intolerance or cold urticaria

If symptomatic control is not achieved, third step is addition and titration of high potency antihistamines as tolerated, such as hydroxyzine or doxepin. The fourth step is referral to a subspecialist for the use of an immunomodulatory agent such as omalizumab or cyclosporine.[10,11] Glucocorticoids could be also help with symptom control in refractory CIU.[9,10] Other agents used in CIU are dapsone, sulfasalazine, hydroxychloroquine, and immunosuppressants (tacrolimus, cyclosporine, sirolimus, and mycophenolate).[9,10] Omalizumab is suggested for patients who do not respond to higher doses of H-1 antihistamine therapy.[9] Omalizumab should be considered for refractory CIU if this is favorable from the standpoint of balancing the potential for benefit with the potential for harm/burden and cost.[9,10] Patients enrolled in pivotal clinical studies were required to have a history of at least 6 months of CIU, presence of hives associated with itching for at least 8 consecutive weeks at any time before enrollment despite current use of H-1 antihistamines, and other urticaria activity assessments.[12]

Safety

The most common adverse events reported in patients 12 years and above with asthma were arthralgia, general pain, fatigue, dizziness, pruritus, dermatitis, and earache. Most common adverse events among pediatric patients treated with omalizumab for asthma included nasopharyngitis, headache, pyrexia, abdominal pain, otitis media, and epistaxis. Omalizumab has a boxed warning due to risk of anaphylaxis. It is also contraindicated in patients with history of hypersensitivity to omalizumab or any ingredients of omalizumab.[1]

REVISIONS	
09-05-2008	Policy added to the bcbsks.com web site.
12-01-2011	Revised Title adding "omalizumab" to read "Xolair (omalizumab) Prior Authorization Criteria"
	Description section updated
	In Policy section: ▪ Wording revised from question format to statement format.
	Rationale section removed
	References section updated

REVISIONS	
04-02-2012	In Policy Section: ▪ In A 5, A 6, and A 7 removed, "medication history includes use of" and added "is currently using" to read: "5. The patient is currently using an inhaled corticosteroid…" "6. The patient is currently using a long-acting β_2-agonist…" "7. The patient is currently using a leukotriene modifier…" ▪ Revised wording in A 9 and B 5 from "The dose is within dosing parameters defined in product labeling OR does not exceed 375 mg every 2 weeks." to "a. The dose is within dosing parameters defined in product labeling OR b. If the recommended dose falls in the "Do Not Dose" range, Xolair will be approved at 375 mg every 2 weeks" ▪ For Section A. Initial use of Xolair, revised Length of Approval from "12 months" to "16 weeks". ▪ In Section B removed the following 3 criteria: "1. Patient is twelve years of age or older 2. The pretreatment IgE level ≥ 30 IU (level provided for review of dose) 4. Allergic asthma has been confirmed by skin testing or in vitro reactivity (RAST) testing" and added the following 2 criteria: "1. The patient has been previously approved for the requested therapy through the PA process 3. The patient is currently on and compliant with standard therapy (such as a combination of an inhaled corticosteroid, long acting beta-2 agonist, leukotriene receptor antagonist, theophylline, oral corticosteroid or an oral beta-2 agonist tablet) OR the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL standard therapies" ▪ Revised chart title of "Xolair Dosing Administration" to "FDA Approved Dosing" ▪ Added "Do Not Dose" to the FDA Approved Dosing chart to clarify the policy intent.
	Rationale section added
	References updated
06-07-2013	Title updated from "Xolair® (omalizumab) Prior Authorization Criteria" to "Xolair® (omalizumab)"
	Description section updated to add FDA Approved Indications and Dosage, and Dosage Adjustment information
	Rationale section reviewed, no updates needed.
	Added Coding section ▪ Added HCPCS code: J2357
	References updated
10-04-2013	In Header: ▪ Link to updated Prior Authorization fax form added.
08-15-2014	Description section updated
	In Policy section: ▪ In Item A 2 clarified the indication of "a. The patient has a diagnosis of asthma OR" ▪ In Item A 2 added the indication of "b. The patient has a diagnosis of chronic idiopathic urticaria" ▪ Bundled criteria for asthma use under Item 3 ▪ In Item A 3 a added "but ≤ 700 IU" to read "The pretreatment IgE level ☐30 IU but ≤ 700 IU (level provided for review of dose)" ▪ In Item A 3 b added "but ≤ 150 kg" to read "The patient's weight is ☐30 kg but ≤ 150 kg (weight provided for review of dose)" ▪ In Item A 3 d added new criteria of "The patient has a baseline FEV1 <80% predicted"

REVISIONS	
	▪ In Item A and B removed the wording "If the recommended dose falls in the "Do Not Dose" range, Xolair will be approved at 375 mg every 2 weeks" and added in Items A 4 b and B 2 d "or does not exceed 375 mg every 2 weeks" to read "The dose is within dosing parameters defined in product labeling or does not exceed 375 mg every 2 weeks" ▪ Added new indication of chronic idiopathic urticaria to read: "5. If chronic idiopathic urticaria, the patient meets ALL of the following: a. The patient has a history of chronic idiopathic urticaria for at least 6 months AND c. The patient has a history of hives and itching AND d. The patient is on maximum H1-antihistamine therapy AND d. The dose is within the FDA labeled dose not to exceed 300 mg every 4 weeks" ▪ In Item A Length of Approval add "for asthma" and "24 weeks for chronic idiopathic urticaria" ▪ In Item B removed "Continued use (renewal) of Xolair will be approved when ALL of:" and added "Renewal Evaluation: when" ▪ In Item B 2 a added "but ≤ 150 kg" to read "The patient's weight is □30 kg but ≤ 150 kg (weight provided for review of dose)" ▪ In Item B 2 removed the wording of "Patient assessment indicates Xolair is contributing to improvement in asthma symptoms or maintenance of asthma control" ▪ Added new indication of chronic idiopathic urticaria to read: "3. If chronic idiopathic urticaria, the patient meets ALL of the following: a. Improvement in symptoms (e.g. number of hives, size of hives, reduction in itching) AND b. The dose is within the FDA labeled dose not to exceed 300 mg every 4 weeks" ▪ Updated the FDA Approved Dosing chart and added "for Asthma" to the chart title.
	Rationale section updated
	References updated
06-01-2015	Policy published 04-21-2015.
	Description section updated
	In Policy section: ▪ In Item A 2 added "The patient has another FDA labeled diagnosis" ▪ In Item A 3 h added "(pre-treatment serum IgE level and body weight)" ▪ In Item A 4 added "c. ONE of the following:" ▪ In Item A 4 c 1) added "currently" and "tolerable" to read "The patient is currently on maximum tolerable H1-antihistamine therapy OR" ▪ In Item A 4 c added "2) The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to H1 antihistamine therapy" ▪ In Item A added the length of approval of: "12 months for all other FDA approved indications" ▪ In Item B revised "Renewal Evaluation: when ALL of the following are met:" to read "Continued use (renewal) of Xolair will be approved when ALL of the following are met:" ▪ In Item B 2 b added "OR" between 1), 2), 3) and 4). ▪ In Item B 2 added "c. ONE of the following:" ▪ In Item B 2 d added "(pre-treatment serum IgE level and body weight)" ▪ In Item B added "4. If another FDA approved diagnosis, the dosing is within the FDA approved dosing limit."
	Rationale section updated
	Coding section removed
	References updated
04-15-2016	Description section updated to include adding Dosing Adjustment information
	In Policy section: ▪ In Item A added "(omalizumab)" to read "Initial use of Xolair (omalizumab)…"

REVISIONS	
	▪ In Item A 1 moved to another section of the policy "Patient is twelve years of age or older" and added "The patient does not have any FDA labeled contraindications to the requested agent." ▪ Added Item 2 a "BOTH of the following" ▪ In Item 2 a i added "The patient has ONE of the following diagnoses:" ▪ In Item 2 a i 1) removed "The patient has a diagnosis of" and added "Moderate to severe persistent" to read "Moderate to severe persistent asthma" ▪ Added Item 2 a ii "The patient is twelve years of age or over" ▪ In Item 2 b removed "labeled" and added "approved" to read "The patient has another FDA approved diagnosis" ▪ In Item 3 added "diagnosis is moderate to severe persistent" to read "If the diagnosis is moderate to severe persistent asthma, the patient meets ALL of the following:" ▪ In Item 3 c added "a positive" and "to a perennial aeroallergen" to read "Allergic asthma has been confirmed by a positive skin test or in vitro reactivity test (RAST) to a perennial aeroallergen" ▪ Added Item 3 e: "e. The patient has ONE of the following: i. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months OR ii. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months OR iii. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered" ▪ Added Item 3 f "ONE of the following" ▪ In Item 3 f i removed "using an" and added "treated with a maximally tolerated" to read "The patient is currently treated with a maximally tolerated inhaled corticosteroid" ▪ In Item g i removed "using a" and added "treated with ONE of the following:" to read "The patient is currently treated with ONE of the following:" Added to Item g i: "2) A Leukotriene receptor antagonist (LRTA) OR 3) Long-acting muscarinic antagonist (LAMA) OR 4) Theophylline" ▪ In Item g ii added "(LABA), leukotriene receptor antagonist (LRTA), Long-acting muscarinic antagonist (LAMA), AND theophylline" to read "The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to long-acting beta-2-agonists agonist (LABA), leukotriene receptor antagonist (LRTA), Long-acting muscarinic antagonist (LAMA), AND theophylline" ▪ Removed "The patient is experiencing exacerbations of asthma symptoms requiring increased inhaled corticosteroid dosing, increased daily use of beta-2-agonist rescue medication or systemic steroids" ▪ In Item 3 h removed "parameters" and "product" and added "requested", "based on", "the patient's", "FDA approved" and "(refer to Table 2) AND" to read "The requested dose is within dosing (based on pre-treatment serum IgE level and the patient's body weight) as defined in FDA approved labeling (refer to Table 2) AND does not exceed 375 mg every 2 weeks" ▪ In Item 4 added "the diagnosis is" to read "If the diagnosis is chronic idiopathic urticaria, the patient meets ALL of the following:" ▪ Added Item 5 "If another FDA approved diagnosis, the dosing is within the FDA approved dosing limit" ▪ In Item B added "(omalizumab)" to read "Continued use of Xolair (omalizumab)…" ▪ Added Item 2 "The patient does not have any FDA labeled contraindications to the requested agent"

REVISIONS	
	▪ In Item 3 added " If the diagnosis is moderate to severe persistent" to read "If the diagnosis is moderate to severe persistent asthma, the patient meets ALL of the following:" ▪ In Item 3 b removed "does not have" and "worsening" and added "has had" and "response or disease stabilization as" to read "The patient has had clinical response or disease stabilization as defined by ONE of the following: ▪ Added Item 3 b i "Increase in percent predicted FEV1 from baseline" ▪ In Item 3 b ii removed "increase in" and "use" and added "Decrease in the does of" and "required to control the patient's asthma" to read "Decrease in the dose of inhaled corticosteroid required to control the patient's asthma" ▪ In Item 3 b iii added "Decrease in need for" to read "Decrease in need for treatment with systemic corticosteroids" ▪ In 3 b removed "Increased use of short acting beta-2-agonist rescue medication" ▪ In 3 b iv removed "Unscheduled care" and "ER, or hospitalizations)" and added "Decrease in number of hospitalizations, need for mechanical ventilation", "to the emergency room or", and "of asthma" to read "Decrease in number of hospitalizations, need for mechanical ventilation, or visits to the emergency room or urgent care due to exacerbations of asthma" ▪ In Item 3 c i removed "on", "such as a combination of an" and "oral corticosteroid or an oral beta 2 agonist tablet" and added "treated" and "(LTRA), Long-acting muscarinic antagonist (LAMA)" to read "The patient is currently treated and is compliant with standard therapy (e.g. inhaled corticosteroids, long acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), Long-acting muscarinic antagonist (LAMA) and theophylline" ▪ In 3 d removed "parameters" and "product" and added "based-on", "FDA approved" and "(refer to Table 2 AND" to read "The dose is within dosing based-on pre-treatment serum IgE level and the patient's body weight as defined in FDA approved labeling (refer to Table 2) AND does not exceed 375 mg every 2 weeks" ▪ In Item 4 added "the diagnosis is" to read "If the diagnosis is chronic idiopathic urticaria, the patient meets ALL of the following:" ▪ In Item 4 b removed "not to exceed" and added "(i.e." to read "The dose is within the FDA labeled dose (i.e. 300 mg every 4 weeks)" ▪ Added Table 1 for Contraindications ▪ Added Table 2: FDA Approved Dosing based on pre-treatment IGE level and body weight
	Rationale section updated
	References updated
01-01-2017	Policy published 12-29-2016. Effective 01-01-2017.
	Description section updated to include replacing FDA Indication and Dosage information with an FDA Approved Indications and Dosage chart.
	Summary of Policy section updates: ✓Added Xolair's new FDA approved indication for treatment of moderate to severe asthma in patients 6 to less than 12 years of age. ✓Extended the initial duration of approval from 16 weeks to 24 weeks. This was due to the new FDA indication mentioned above. ✓Added requirement that Xolair will not be used in combination with an injectable IL-5 inhibitor indicated for asthma (e.g. Nucala) ▪ These updates resulted in the following policy language changes: <u>Initial Use</u> ▪ Added Item A 2 "The requested agent will not be used with an injectable IL-5 inhibitor indicated for asthma (e.g. Nucala, Cinqair)" ▪ Removed "The patient is twelve years of age or over" ▪ Added Item 4 a "If the patient is 6 to less than 12 years of age, the patient meets BOTH of the following:" ▪ In Item 4 a i added "to 1300 IU/mL" and removed "but ≤ 700 IU (level provided for review of dose)" to read "The pretreatment IgE level is 30 IU/mL to 1300 IU/mL"

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	▪ In Item 4 a ii added "20" and removed "≥ 30" and "(weight provided for review of dose) to read "The patient's weight is 20 kg to 150 kg" ▪ Added Item 4 b "If the patient is 12 years of age and above, the patient meets ALL of the following: i. The pretreatment IgE level is 30 IU/mL to 700 IU/mL AND ii. The patient's weight provided for review of dose)is 30 kg to 150 kg AND iii. The patient has a baseline FEV1 <80% predicted" ▪ In Item 5 c removed "The patient has a baseline FEV1 <80% predicted" ▪ In Item 5 removed "The patient is 12 years of age or above" ▪ In Length of Approval removed "16 weeks for asthma" and added "asthma and" to a separate length of approval phrase to read "24 weeks for asthma and chronic idiopathic urticaria" <u>Continued Use (renewal)</u> ▪ Added Item B 3 "The requested agent will not be used in combination with an injectable IL-5 inhibitor indicated for asthma (e.g. Nucala, Cinqair)" ▪ In Item 4 a removed "≥", "but ≤", "(weight provided for review of dose)" and added "within the FDA indicated range for their age (i.e. 20 kg to 150 kg for patients age 6 to less than 12 years and" and "(for patients 12 years of age and above)" to read "The patient's weight is within the FDA indicated range for their age (i.e. 20 kg to 150 kg for patients age 6 to less than 12 years and 30 kg to 150 kg (for patients 12 years of age and above)" ▪ Added Table titled "FDA Approved Dosing for Patients Age 6 to less than 12 Years" ▪ Revised title to Pre-treatment Serum IgE and Body weight table to " FDA-Approved Dosing for Patient 12 years of Age and Above"
	Rationale section updated
	References updated
05-15-2017	Description section updated
	In Policy section: ▪ In Item B removed "If another FDA approved diagnosis, the dosing is within the FDA approved dosing limit." to clarify another FDA approved diagnosis is part of the initial criteria and not required in the renewal criteria.
	Rationale section updated
	References updated
05-01-2018	Description section updated
	In Policy section: <u>Initial Evaluation</u> ▪ In Item 1 A v a, 1 A vi a and 1 B iv a added "in the past 90 days" ▪ In Item 1 C removed "approved dosing limit" and added "for the requested agent AND the requested dose" and "labeled dose" to read "The patient has another FDA approved diagnosis for the requested agent AND the requested dose is within the FDA labeled dose" <u>Renewal Evaluation</u> ▪ In Item 2 A ii c added "due to exacerbations of asthma" to read "Decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma ▪ In Item 2 A iii a added "in the past 90 days " ▪ In Item 2 A iv "removed "within dosing" and added "requested" to read "The requested dose is based-on pre-treatment serum IgE level and the patient's body weight as defined in FDA approved labeling AND does not exceed 375 mg every 2 weeks" ▪ In Item 2 B ii added "requested" and "AND does NOT exceed" to read "The requested dose is within the FDA labeled dose AND does NOT exceed 300 mg every 4 weeks" ▪ Added Item 2 C "The patient has another FDA approved diagnosis for the requested agent AND the requested dose is within the FDA labeled dose for the requested indication"
	Rationale section updated

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	References updated
11-01-2018	Description section updated to include FDA Approved Indications and Dosage chart updated
	In Policy section: Summary of changes: • For diagnosis of asthma, additional option for patients who have already been treated with Xolair, review if on an inhaled corticosteroid that is dosed to control symptoms rather than be on maximally tolerated inhaled corticosteroid • For diagnosis of chronic idiopathic urticaria (CIU): o Removal of 6 months history of CIU o Addition for prerequisites to TWO different CIU therapies for at least 2 weeks. Xolair is considered after failure of prerequisites in guidelines o Removal of "currently on maximally tolerated H1 antihistamine therapy in the past 90 days" – as prerequisites should be sufficient rather than current therapy • Addition of specialist Initial Evaluation ▪ In Item I A v a added "is NOT currently being treated with the requested agent AND" to read "The patient is NOT currently being treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid in the past 90 days" ▪ In Item I A v added "b. The patient is currently being treated with the requested agent AND is currently treated with an inhaled corticosteroid that is dosed as needed to control symptoms" ▪ In Item 1 B ii removed "The patient is currently on maximally tolerated H1-antihistamine therapy within the past 90 days" ▪ In Item 1 B ii added "a. The patient has tried and had an inadequate response to TWO different classes of CIU therapies for at least 2 weeks duration of each course (first generation H-1 antihistamine [doxepin, hydroxyzine, cyproheptadine], second generation H-1 antihistamine [cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine], H-2 antihistamine [ranitidine, famotidine, cimetidine], leukotriene receptor antagonist [montelukast, zafirlukast])" ▪ In Item 1 B 2 b removed "H1 antihistamine therapy" and added "ALL prerequisite agents" to read "The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL prerequisite agents" ▪ Added "2. The prescriber is a specialist (e.g. allergist, immunologist, pulmonologist) in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis" Renewal Evaluation ▪ Added "3. The prescriber is a specialist (e.g. allergist, immunologist, pulmonologist) in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis"
	Rationale section updated
	References updated
12-03-2018	Policy published 01-01-2019. Policy retro-effective to 12-03-2018.
	Addition of prefilled syringes of Xolair as targets

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