

## Corporate Medical Policy

### Xolair® (Omalizumab)

<b>File Name:</b>	xolair_omalizumab
<b>Origination:</b>	9/2003
<b>Last CAP Review:</b>	11/2011
<b>Next CAP Review:</b>	11/2012
<b>Last Review:</b>	4/2012

#### Description of Procedure or Service

---

Asthma is a chronic lung disease that affects an estimated 20 million Americans. Asthma is characterized by inflammation of the airways. The inflammation makes the airways smaller which makes it more difficult for air to move in and out of the lung, creating the symptoms of asthma (cough, chest tightness, shortness of breath and wheezing). The severity of asthma varies from mild intermittent to severe persistent. Asthma is related to a number of factors, including family history, smoking, stress and allergies. In the initial assessment and diagnosis of asthma, the following must be determined:

- History or presence of episodic symptoms of airflow obstruction (i.e., wheezing, shortness of breath, chest tightness, or cough);
- Airflow obstruction is at least partially reversible (demonstration of reversibility, defined as > 12% improvement and 200 mL increase in FEV1, or a 20% increase in PEF following the inhalation of a bronchodilator);
- Alternative diagnoses are excluded (e.g., vocal cord dysfunction, vascular rings, foreign bodies, or other pulmonary diseases).

For some patients, allergies play a significant role in their asthma. Allergic asthma is the most common form of asthma, affecting over 50% of the 20 million asthma sufferers. Many of the symptoms of allergic and non-allergic asthma are the same (coughing, wheezing, shortness of breath or rapid breathing, and chest tightness). However, allergic asthma can be triggered by several factors, including inhaled allergens such as dust mite allergen, pet dander, pollen, mold, etc. resulting in asthma symptoms. Other factors that may trigger asthma symptoms are irritants such as tobacco smoke and strong odors, weather changes, viral or sinus infections, exercise, reflux disease, medication or foods.

Allergens are identified as a key cause of allergic asthma; however, the real culprit in causing allergic asthma is the IgE (immunoglobulin E) antibody. The IgE antibody is produced by the body in response to allergen exposure. The combination of the IgE antibody with allergens results in the release of potent chemicals called mediators. The mediators cause the inflammation and swelling of the airways, resulting in the symptoms of asthma. This makes the antibody IgE an underlying cause of allergic asthma symptoms. Anti-IgE antibody treatments are a new type of preventative drug therapy used to reduce asthma symptoms. Anti-IgE antibody treatments disrupt the sequence of events that causes the allergic reaction.

Xolair® (Omalizumab) is the first asthma treatment that works by blocking IgE (anti-IgE antibody treatment). Xolair® is a recombinant DNA-derived humanized monoclonal antibody that selectively binds to human IgE and inhibits the immune system's response to allergen exposure. Thus,

# Xolair® (Omalizumab)

inflammation is blocked at the initiation stage. It is indicated for adults and adolescents with moderate to severe persistent asthma. It has been shown to be beneficial as adjunctive therapy in patients whose symptoms are inadequately controlled despite appropriate therapy for moderate to severe asthma. Xolair® is to be prescribed as prophylactic therapy for allergy-induced asthma. It is to be used in conjunction with other agents used in the management of moderate to severe persistent asthma, but never as monotherapy.

**Xolair® is effective in the treatment of allergy-induced asthma only.** Allergy tests are required to identify patients who may be candidates for Xolair® therapy. The FDA advisory committee defines having allergic asthma as testing positive to at least one perennial aeroallergen according to either a skin test (e.g., prick/puncture test, intracutaneous test) or a blood test (e.g., RAST) and having an IgE level between 30 and 700 IU/mL. The use of Xolair® in patients with IgE levels less than 30 and greater than 700 IU/mL has not been adequately studied and should not be used.

Xolair® has not been shown to alleviate asthma exacerbations acutely and should not be used for treatment of acute bronchospasm or status asthmaticus. Patients should have a short-acting beta2-agonist available for rescue therapy.

***\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

## Policy

---

**BCBSNC will provide coverage for Xolair® when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

## Benefits Application

---

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Members may also be eligible to participate in BCBSNC's Member Health Partnership Program for Asthma. Verify eligibility and if eligible, refer member to Member Health Partnerships.

## When Xolair® (Omalizumab) is covered

---

### A. Initial Coverage Review:

Xolair® is indicated for adults and adolescents (12 years of age and above) with **ALL** of the following:

1. moderate to severe **persistent** asthma; **and**
2. positive skin test or in vitro reactivity to a perennial aeroallergen; **and**
3. symptoms are inadequately controlled despite use of medium dose of inhaled corticosteroids with combination therapy (long acting inhaled B2 agonist or leukotriene modifier) for at least three months, **OR** there is a requirement for chronic administration of systemic corticosteroids or high dose inhaled corticosteroids to maintain adequate control; **and**
4. IgE level >30 but < 700 IU/mL.

# Xolair® (Omalizumab)

## B. Continuation of coverage after 12 months:

Documentation must be provided of continued symptom improvement and/or decreased exacerbations and/or decreased use of rescue medications based on physician re-evaluation every 12 months thereafter.

Patients undergoing treatment with Xolair® prior to the effective date of coverage under a BCBSNC health plan, will meet BCBSNC criteria if the treating physician certifies that initial coverage criteria under A. above were met prior to initiation of therapy.

## When Xolair® (Omalizumab) is not covered

---

Xolair® (Omalizumab) is considered not medically necessary when the conditions listed above have not been met.

Xolair® has not been shown to alleviate asthma exacerbations acutely and should not be used for the treatment of acute bronchospasm or status asthmaticus.

Xolair® is considered not medically necessary for allergic rhinitis.

## Policy Guidelines

---

Because the use of Xolair® (Omalizumab) requires allergy testing and assessment of IgE blood levels prior to its use, initial administration or prescription should be given by a consulting specialist (pulmonologist or allergist) with significant training and experience in the diagnosis and treatment of asthma and allergies.

According to the NHLBI, patients with **moderate persistent asthma** exhibit some of the following characteristics:

- Daily symptoms
- Daily use of inhaled short-acting beta2-agonists
- Exacerbations affect activity
- Exacerbations > 2 times a week; may last days
- Nighttime symptoms >1 time a week
- FEV1 or PEF more than 60% but less than 80% predicted
- PEF variability >30%

Patients with **severe persistent asthma** exhibit some of the following characteristics:

- Continual symptoms
- Limited physical activity
- Frequent exacerbations
- Frequent nighttime symptoms
- FEV1 or PEF  $\leq$  60% predicted
- PEF variability >30%

Clinical documentation of inadequately controlled symptoms (#3 under "When Covered") includes frequent severe exacerbations that often require emergency room visits, unscheduled office visits and/or hospitalizations, excessive use of rescue medications and/or oral steroids, impairment in activities of daily living, such as work, school, exercise and/or sleep.

Due to an expected delayed onset of action, the efficacy of Xolair® is determined after treatment for

# Xolair® (Omalizumab)

a minimum of 12 weeks.

In February 2007 the FDA requested that the product label for omalizumab include a boxed warning emphasizing that Xolair® may cause anaphylaxis. Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, usually occurred within two hours of receiving the subcutaneous injection. However, there have been reports of delayed anaphylaxis with onset two to 24 hours after treatment. Anaphylaxis may occur after any dose of Xolair® (including the first dose), even if the patient had no allergic reaction to the first dose. Health care professionals should observe patients for at least two hours after Xolair® is given and should be prepared to manage life-threatening anaphylaxis.

Health care professionals should educate patients using Xolair® about the risk of anaphylaxis and educate those patients on how to recognize and treat Xolair® induced anaphylaxis. Patients using Xolair® should be educated about, and prescribed, an epinephrine autoinjector device (Epi-pen, or similar device.)

## Billing/Coding/Physician Documentation Information

---

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: J2357*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

---

Milgrom H, Berger W, Nayak A, Gupta N, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (Omalizumab). *Pediatrics*. August 2001; 108(2). Retrieved from <http://www.pediatrics.org/cgi/content/full/109/2/e36>

Rosenwasser, LJ and Nash, DB. Incorporating omalizumab into asthma treatment guidelines: consensus panel recommendations. *P & T*. June 2003, 28(6):400-410.

Specialty Matched Consultant - 9/2003

Medical Policy Advisory Group - 10/2003

ECRI Hotline Response - Omalizumab (Xolair) for the Treatment of Allergic Asthma (07/28/2003) retrieved on 6/4/04 from [http://www.ta.ecri.org/Hotline/prod/summary/detail.aspx?doc\\_id=7012](http://www.ta.ecri.org/Hotline/prod/summary/detail.aspx?doc_id=7012)

ECRI Target Report #863 (2004, May) Omalizumab (Xolair) to treat pediatric allergic asthma.

Retrieved on June 4, 2004 from [http://www.target.ecri.org/summary/detail.aspx?doc\\_id=5409](http://www.target.ecri.org/summary/detail.aspx?doc_id=5409).

Specialty Matched Consultant Advisory Panel - 7/2004

Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. NIH Publication No. 02-3659 Issued January 1995 (updated 2002, 2003, 2004; accessed 6/29/05).

# Xolair® (Omalizumab)

Available at: <http://www.ginasthma.com/Guidelineitem.asp?l1=2&l2=1&intId=60>.

National Asthma Education and Prevention Program: Expert Panel Report 2: Guidelines for the diagnosis and management of asthma. NIH Publication No. 97-4051. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>. Bethesda, Md: National Institutes of Health; 1997.

Specialty Matched Consultant Advisory Panel - 6/17/05

Specialty Matched Consultant Advisory Panel - 7/27/06

U.S. Food and Drug Administration. Product Approval Information - Licensing Action. Retrieved on September 6, 2006 at <http://www.fda.gov/cder/biologics/products/omalgen062003.htm>

U.S. Food and Drug Administration. Label and Approval History with 6/20/2003 and 4/7/2006 approval information. Retrieved on September 7, 2006 at [http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label\\_Approval\\_History#aphist](http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_Approval_History#aphist)

Xolair® (Omalizumab) Prescribing Information. Retrieved 5/28/08 from <http://www.xolair.com/pdf/xolair-prescribing.pdf>

National Institute for Clinical Guidance (NICE). Guidance on Omalizumab for severe persistent allergic asthma. Technology Appraisal Guidance 133. London, UK: NICE; November 2007. Available at <http://www.nice.org.uk/nicemedia/pdf/TA133Guidance.doc>

U.S. Food and Drug Administration. FDA News. FDA proposes to strengthen label warning for Xolair. Retrieved 3/9/07 from <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01567.html>

Global Initiative for Asthma® (GINA), National Heart, Lung and Blood Institute (NHLBI), World Health Organization (WHO). Global strategy for asthma management and prevention. Global Initiative for Asthma (GINA). Bethesda, MD. February 2002. Updated 2009. Retrieved on October 17, 2010 from: <http://www.ginasthma.com/Guidelineitem.asp?l1=2&l2=1&intId=1561>

Morjaria JB, Polosa R. Off-label use of omalizumab in non-asthma conditions: new opportunities. Abstract. Expert Rev Respir Med. 2009 Jun;3(3):299-308. Retrieved on October 18, 2010 from <http://www.ncbi.nlm.nih.gov/pubmed/20477322>

National Institutes of Health (NIH). Omalizumab in the Treatment of Peanut Allergy. Clinical Trial Identifier NCT00949078. Reviewed on October 27, 2011 from <http://clinicaltrials.gov/ct2/show/NCT00949078>

National Institutes of Health (NIH). Subcutaneous Omalizumab for Treatment of Chronic Rhinosinusitis With Nasal Polyposis (Xolair CRS). Clinical Trial Identifier NCT01066104. Reviewed on October 27, 2011 from <http://clinicaltrials.gov/ct2/show/NCT01066104>

Specialty Matched Consultant Advisory Panel review 11/2010

Specialty Matched Consultant Advisory Panel review 11/2011

## Policy Implementation/Update Information

---

9/03 Original policy issued.

10/03 Source added. Spell check.

---

# Xolair® (Omalizumab)

11/03 Medical Policy Advisory Group review. No change to the policy.

3/04 Code S0107 added to the policy.

10/14/04 Specialty Matched Consultant Advisory Panel review 7/23/2004. Inadequately controlled asthma defined in "Policy Guidelines". Sources added.

1/6/05 First quarter 2005 HCPCS code J2357 added to the Billing/Coding section of policy.

8/4/05 Specialty Matched Consultant Advisory Panel review 6/17/05. "Description" section revised. Under "Benefits Application" section, added information re: Member Health Partnership Program for Asthma. "When Covered" section separated into initial coverage review, continuation of coverage review beyond 6 months and after 12 months. Also #5 re: evidence of reversible disease deleted from this section and incorporated into the "Description" section regarding the initial assessment and diagnosis of asthma. Policy Guidelines expanded to list characteristics exhibited with moderate persistent asthma and severe persistent asthma. Notice given 8/4/05. Effective date 10/6/05.

10/8/05 HCPCS code S0107 is no longer valid as of 01/01/05. Code S0107 removed from Billing/Coding section. Due to a scheduling change for the 10/6/05 website update, the effective date for the 8/4/05 entry above is 10/8/05.

10/2/06 Specialty Matched Consultant Advisory Panel review 7/2006. Reference sources added. No changes to criteria. (pmo)

8/25/08 The following was added to the Policy Guidelines section: "In February 2007 the FDA requested that the product label for omalizumab include a boxed warning emphasizing that Xolair® may cause anaphylaxis. Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, usually occurred within two hours of receiving the subcutaneous injection. However, there have been reports of delayed anaphylaxis with onset two to 24 hours after treatment. Anaphylaxis may occur after any dose of Xolair® (including the first dose), even if the patient had no allergic reaction to the first dose. Health care professionals should observe patients for at least two hours after Xolair® is given and should be prepared to manage life-threatening anaphylaxis. Health care professionals should educate patients using Xolair® about the risk of anaphylaxis and educate those patients on how to recognize and treat Xolair® induced anaphylaxis. Patients using Xolair® should be educated about, and prescribed, an epinephrine autoinjector device (Epi-pen, twin-ject)." References updated. Specialty Matched Consultant Advisory Panel review 7/14/08. No change to policy statement. (adn)

6/22/10 Policy Number(s) removed (amw)

12/21/10 Specialty Matched Consultant Advisory Panel review 11/2010. References updated. (mco)

12/20/11 Specialty Matched Consultant Advisory Panel review 11/2011. Revised following statement from "Description" section: "It has been shown to be beneficial as adjunctive therapy in patients whose symptoms are inadequately controlled despite the regular use of maximum dose inhaled corticosteroids." to "It has been shown to be beneficial as adjunctive therapy in patients whose symptoms are inadequately controlled despite appropriate therapy for moderate to severe asthma." Removed the following statement from the "When Covered" section: "Depending on the length of time the patient has been receiving Xolair® therapy, documentation may be necessary to verify that criteria for continuing therapy are met (under B. and/or C. above.)" Revised the following statement in the "When not Covered" section: "Xolair® (Omalizumab) is not covered when the conditions listed above have not been met." to "Xolair® (Omalizumab) is considered **not medically necessary** when the conditions listed above have not been met." Removed "twin-ject" from Policy Guidelines and replaced with "or similar device." References updated. (mco)

## Xolair® (Omalizumab)

5/15/12 Deleted sections B1 and 2 from “When Covered” section addressing continuation of coverage after 6 months. Continuation of Xolair will be reviewed after 12 month interval. Medical Director review 4/2012. (mco)

---

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.