Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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Category: Medicine
***Current Policy Effective Date: 1/1/09**

Title: Xolair® (Omalizumab RhuMAb-E25) Procedure Code(s): J2357

Description/Background

Asthma is a chronic inflammatory condition of the airways that includes symptoms of wheezing, breathlessness and nighttime awakenings. The symptoms range from mild to severe and may necessitate hospitalization. Responses may be connected to specific IgE (allergic) or unidentifiable (non-allergic) in nature. There is no standard definition of allergic asthma. It has been defined as a chronic inflammatory disorder of the airways. Its symptoms are made worse by exposure to an allergen (i.e., dust, mold, pollen or animal dander) to which the patient has been sensitized.

Xolair® (Omalizumab) is a recombinant Chinese hamster ovary cell-derived IgG1 kappa humanized monoclonal antibody produced by Genentech, Tanox and Novartis for the treatment of allergic asthma. Xolair® was approved by the U.S. Food and Drug Administration (FDA) in June 2003. It inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils. The release of mediators to an allergic response is thus limited, resulting in a lower incidence of asthma exacerbations in adults and adolescents with moderate to severe persistent asthma that is characteristically provoked by specific aeroallergens.

Allergens are identified as a key cause of allergic asthma, but 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

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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, 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 the regular use of maximum dose inhaled corticosteroids. Xolair® is to be prescribed as prophylactic therapy for allergy-induced asthma. It is never used as monotherapy.

Xolair® was evaluated in three randomized, double blind, placebo-controlled, multicenter trials. The studies enrolled 1,412 patients, aged 12-76 years with moderate to severe persistent asthma and a positive skin test reaction to a perennial aeroallergen.

Asthma severity may be classified by clinical features (from the Global Initiative for Asthma) as follows:

A. Intermittent
- Number of symptoms per week (less than one symptom per week, asymptomatic otherwise)
- Brief exacerbations
- Nocturnal symptoms not more than twice/month
- FEV_1 ≥80% predicted or PEF ≥80% of personal best
- PEF or FEV_1 variability <20%

B. Mild Persistent
- Symptoms more than once/week but less than once/day
- Exacerbations may affect activity and sleep
- Nocturnal symptoms more than twice/month
- FEV_1 ≥80% predicted or PEF ≥80% of personal best
- PEF or FEV_1 variability 20% to 30%

C. Moderate Persistent
- Symptoms daily
- Exacerbations may affect activity and sleep
- Nocturnal symptoms more than once/week
- Daily use of inhaled short-acting $beta_2$-agonist
- FEV_1 (forced expiratory volume) 60% to 80% predicted or PEF (peak expiratory flow) 60% to 80% of personal best
- PEF or FEV_1 variability >30%

D. Severe Persistent
- Symptoms daily
- Frequent exacerbations

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- Frequent nocturnal asthma symptoms
- Limitation of physical activities
- $FEV_1 \leq 60\%$ predicted or PEF $\leq 60\%$ of personal best
- PEF or FEV_1 variability >30%

Xolair® is administered subcutaneously every two or four weeks. Xolair® must be dissolved in sterile water for injection, and takes 15 to 20 minutes to dissolve. The injection may take five to ten seconds to administer since the solution is slightly viscous. Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair. Health care providers administering Xolair® should be prepared to manage anaphylaxis that can be life threatening. Xolair® should not be self-administered.

CPT / HCPCS Level II Codes and Description *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

J2357 Injection, omalizumab, 5 mg

Diagnoses / Medical Conditions

- Extrinsic asthma
- Allergic asthma with stated cause

Medical Policy Statement

The safety and effectiveness of Xolair® have been established. It may be considered a useful therapeutic option for patients meeting specific patient selection criteria.

Rationale

Xolair has been shown to be an effective treatment for patients with moderate to severe allergic asthma (caused by perennial aeroallergens) who have not responded adequately to maximum medical management with other medications or treatments.

In a randomized controlled clinical trial (RCCT) study, published in *The American College of Chest Physicians* in 2004 by Bousquet, et al., 1,070 adults and adolescents with allergic asthma were studied. The conclusion of the study was that patients who benefited the most from omalizumab given as an add-on therapy were patients who

- Were receiving high doses of beclomethasone dipropionate (BDP) [≥ 800 µg/d].

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- Have a history of frequent emergency asthma treatment (omalizumab has the potential to reduce asthma exacerbations by one-half and improve disease control).
- Have poor lung function (≤ 65%).

A trial of omalizumab should last a minimum of 12 weeks.

Holgate, et al., in a March 2005 article published in the *Journal of the American Academy of Allergy, Asthma and Immunology,* entitled, "The anti-inflammatory effects of omalizumab confirm the central role of IgE in allergic inflammation" found that "omalizumab has a central role in inhibiting the allergic inflammatory cascade." The evidence supports the fact that Xolair® has a pronounced effect on the underlying inflammatory state and a preventive effect on the worsening inflammation (on allergen exposure) that underlies asthma flares or exacerbations.

An article in the 2005 *Medscape General Medicine* by Belliveau, "Omalizumab: A Monoclonal Anti-IgE Antibody," relates the results of clinical trials for diagnoses concomitant with asthma and other conditions such as allergic rhinitis, severe allergic rhinitis (SAR), perennial allergic rhinitis (PAR) and concomitant asthma and PAR.

In a randomized trial of 23 patients in 2004, published in the European *Respiratory Journal,* Hanf et al., found that after 16 weeks of treatment with subcutaneous omalizumab, nasal scores following a nasal allergen challenge were significantly lower in omalizumab recipients compared to placebo recipients.

The first randomized, placebo-controlled, double-blinded studies with ragweed-induced SAR had too few patients and did not demonstrate adequate IgE suppression, possibly due to the numbers. The second ragweed-induced trial was completed by Cassale, et al., "Effect of omalizumab on symptoms of seasonal allergic rhinitis. A randomized controlled trial," published in *JAMA*, Vol. 286, 2001.

Note**:** Due to the complicated reconstitution of this subcutaneous medication (it takes approximately ten to twenty minutes) and the potential for severe reactions (e.g., anaphylaxis) extending beyond first and second doses, it cannot be self-administered in the home. It should be administered in the physician's office.

Medical Policy Position Summary (Non-clinical summary statement for customer use)

Xolair® was approved by the U.S. Food and Drug Administration (FDA) in June 2003.

Xolair® is an effective treatment for patients with specific moderate to severe persistent allergic asthma who have tried multiple treatments for their symptoms without adequate relief. It is given by subcutaneous (under-the-skin) injection on a schedule and dosage determined by the treating doctor. It should be given in the doctor's office due to the complex nature of the mixing of the medication and possible side effects.

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The safety and effectiveness of Xolair® have been established. It may be considered a useful therapeutic option for patients meeting specific patient selection criteria.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

A. Initial Review:
Xolair® is indicated for adults and adolescents (12 years of age and above) with **ALL** of the following:
- A diagnosis of moderate to severe persistent asthma
- Positive skin test or in-vitro reactivity to a perennial aeroallergen
- 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
- There is a requirement for chronic administration of systemic corticosteroids or high dose inhaled corticosteroids to maintain adequate control; **and**
- IgE level >30 but < 700 IU/mL.

B. Continuation of coverage for Xolair® beyond 6 months may be appropriate in the following situations:
- The patient has not experienced an adverse reaction to Xolair® therapy; **and**
- The patient has experienced improved symptom control and/or decreased exacerbations on physician re-evaluation at 4-6 months.

C. 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 3-6 months thereafter.

Prior to initiation of treatment with Xolair® the member should have documentation of three months of maximum medical treatment of allergic asthma and meet all of the following criteria:
- Documentation of a consult with an allergist /immunologist or pulmonologist prior to initiation of Xolair therapy to confirm the diagnosis of uncontrolled moderate to severe allergic asthma.
- Verification in the medical record of the member following National Heart, Lung and Blood Institute (NHLBI) published Guidelines for the Diagnosis and Management of Asthma.
- Positive diagnostic evidence established by either skin or blood test to a specific aeroallergen (IgE) before therapy is initiated.
- Evidence of reversible disease with bronchodilators (>12% increase in FEV_1 with at least a 200 ml increase).

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- Documented failure of adequate trials of first-line therapies at maximum doses to include corticosteroids in combination with other established treatment modalities such as long/short acting β-agonists and leukotriene inhibitors.
- Verifiable compliance to maximum medical management for a minimum of three (3) months.
- Documentation of informed consent regarding post-market surveillance studies.
- Between 30 and 150 kg (approximately 66 to 330 pounds) in body weight with a serum IgE 30 to 700 IU/mL.
- If female, non-pregnant/non-lactating.
- Current non-smoker.

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 < 30 and > 700 IU/mL has not been adequately studied and should not be used.

A one-year trial with Xolair® is suggested after which tapering should begin. If the patient continues to experience allergic asthma exacerbations after one year, the patient is classified as a non-responder and Xolair® treatment should be discontinued**.**

Related Policies

N/A

Medicare Information

Indications:

Omalizumab is approved by the Food and Drug Administration (FDA) for patients (12 years of age or above) with moderate to severe persistent asthma who have had a positive skin test or in-vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

Limitations:

Because of the chance of anaphylaxis with omalizumab, patients should receive omalizumab treatment in a doctor's office or clinic setting and be observed for an appropriate period of time after each treatment. Omalizumab should only be administered in a healthcare setting by healthcare providers prepared to manage anaphylaxis that can be life threatening.

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

Utilization:

- Omalizumab 150 to 375 mg is administered subcutaneously every 2 or 4 weeks.
- Omalizumab is covered when the drug is administered by a physician or incident to a physician's service in a clinic or office setting and used in accordance with FDA-approved indications.
- Omalizumab is not covered if self-administered by the patient.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicaid Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

References

- Belliveau, P. P. and M. R. Lahoz, "Evaluation of omalizumab from a health plan perspective," *J Manag Care Pharm,* Volume 11, Number 9, November 1, 2005, pp. 735-745.
- Corren, Jonathan, et al., "Allergen skin tests and free IgE levels during reduction and cessation of omalizumab therapy," *J Allergy Clin Immunol*, Volume 121, Number 2, February 1, 2008, pp. 506-511.
- Hamilton, Robert G., PhD, DABMLI, "Accuracy of US Food and Drug Administration-cleared IgE antibody assays in the presence of anti-IgE (omalizumab)," *J Allergy Clin Immunol*, Volume 117, Number 4, April 2006, pp. 759-766.
- *Hayes Medical Technology Alert,* "Anti-immunoglobulin E Therapy for Severe Allergic Reaction," Volume VI, Number 4, June 2003.
- Hayes *Medical Technology Alert*, "Omalizumab for Allergic Asthma," Volume VI, Number 6, June 2003.
- Holgate, Stephen, MD, et al., "Omalizumab, a novel anti-IgE therapy in allergic disorders," *Expert Opin Biol Ther*, Volume 1, Number 6, pp. 1049-1058.
- Holgate, Stephen, MD, et al., "The anti-inflammatory effects of omalizumab confirm the central role of IgE in allergic inflammation," *J Allergy Clin Immunol*, Volume 115, Number 3, pp. 459-465.
- Krishnan, Jerry A., MD, PhD, and Michael Gould, MD, MS, "Omalizumab for severe allergic asthma: Dollars and sense," *J Allergy Clin Immunol*, Volume 120, Number 5, November 1, 2007, pp. 1015-1017.
- Marcus Philip, MD, "Incorporating Anti-IgE (**Omalizumab**) Therapy Into Pulmonary Medicine Practice," Practice Management Committee, American College of Chest Physicians, *Chest*, Volume 129, Number 2, February 1, 2006, pp. 466-474.
- National Asthma Education and Prevention Program Expert Panel, *Expert Panel Report 3*, "Guidelines for the Diagnosis and Management of Asthma," *NIH Publication Number 08-*

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5846, October 2007, < http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf > (accessed 8/15/08).

- *National Government Services*, "Article for OMALIZUMAB (e.g., Xolair®)," Article ID number A46088, effective date 12/1/07, article ending effective date 08/17/2008, http://www.ngsmedicare.com/NGSMedicare/nyorkpolicya/policy/l25820_att13.htm (accessed 8/15/08).
- Noga, Oliver, MD, et al., "Effect of omalizumab treatment on peripheral eosinophil and T-lymphocyte function in patients with allergic asthma," *J Allergy Clin Immunol,* Volume 117, Number 6, June 1, 2006, pp. 1493-1499.
- Wu, Ann C., et al., "Cost-effectiveness of omalizumab in adults with severe asthma: Results from the Asthma Policy Model," *J Allergy Clin Immunol*, Volume 1146, Number 2, November 1, 2007, pp. 1146-1152.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 8/15/08, the date the research was completed.

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Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/25/04	5/25/04	6/29/04	Joint policy established
7/5/05	7/5/05	7/22/05	Routine maintenance
11/1/06	8/25/06	09/16/06	Routine maintenance
1/1/09	10/13/08	10/13/08	Routine maintenance; policy retired

Next Review Date: This is an established policy and no longer subject to routine review.

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: N/A	Revised: N/A
BCBSM: N/A	Revised: N/A

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BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: XOLAIR® (OMALIZUMAB RHUMAB-E25)

I. Short Description

Xolair® (Omalizumab) is a recombinant Chinese hamster ovary cell-derived IgG1 kappa humanized monoclonal antibody for the treatment of allergic asthma. Its use results in a lower incidence of asthma exacerbations in adults and adolescents with moderate to severe persistent asthma that is characteristically provoked by specific aeroallergens.

Xolair® is administered subcutaneously every two or four weeks. Anaphylaxis has been reported to occur after administration of Xolair. Health care providers administering Xolair® should be prepared to manage anaphylaxis that can be life threatening. Xolair® should not be self-administered.

II. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria applies
BCNA (Medicare Advantage)	Covered; criteria applies
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service. Exception: If BCN65 member has an "exact-fill" option, BCN may cover the service even if Medicare does not.
BlueCaid	Covered; criteria applies

III. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate benefits and certificate riders.
- Appropriate copayments will apply. Refer to certificate section, "*Diagnostic and Therapeutic Services*" and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.

IV. Effective Dates:

Policy updated: 7/5/05, 11/1/06, 1/1/09
Joint policy effective date: 5/25/04

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