BlueCross BlueShield of Alabama

Name of Policy:
Xolair™ (Omalizumab)

Policy #: 131
Category: Pharmacology

Latest Review Date: September 2013
Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Proprietary Information of Blue Cross and Blue Shield of Alabama

Description of Procedure or Service:

Xolair™ is a recombinant DNA-derived humanized IgG1K monoclonal antibody that selectively binds to human IgE.

Xolair™ 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.

Xolair™ is approved by the Food and Drug Administration (FDA) for the treatment of adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Xolair™ has been shown to decrease the incidence of asthma exacerbations in these patients. Safety and efficacy have not been established in other allergic conditions.

Xolair™ 150-375 mg is administered subcutaneously every two or four weeks. The solution is slightly viscous and may take 5 to 10 seconds to administer. The milligrams and dosing frequency are determined by serum total IgE level measured before the start of treatment, and body weight. Injections are limited to 150 mg per injection site.

Xolair™ is not FDA-approved for use in children under the age of 12. In 2011, the FDA Pediatric Advisory Committee conducted a pediatric focused safety review of omalizumab. The committee found that, due to the risk of anaphylaxis and malignancy seen in adult and adolescent patients treated with omalizumab and the modest efficacy of omalizumab seen in the randomized controlled trial in six to <12 years patient, the risk-benefit assessment does not support the use of omalizumab in patients six to 11 years of age.

There has been emerging evidence supporting the off-label use of omalizumab for urticaria. Clinical studies have demonstrated improved disease control, as reflected by a decrease in the weekly urticarial activity score (UAS7), in patients with moderate to severe chronic urticaria treated with omalizumab compared to placebo. However, consensus guidelines on chronic urticarial from leading allergy and immunology organizations classify omalizumab as fourth-line therapy for the treatment of chronic urticarial, it should only be considered for the treatment of patients who have failed or who are unable to use the recommended first-, second-, and third-line treatments (high-dose antihistamines, LTRAs, H2-antagonists, anti-inflammatory agents, and immunosuppressants).

Policy:

Effective for dates of service on or after November 8, 2013:

Xolair™ for the treatment of MODERATE TO SEVERE PERSISTENT ASTHMA meets Blue Cross and Blue Shield of Alabama's medical policy for coverage when initially prescribed by a pulmonologist or allergist/immunologist and when **ALL** of the following criteria are met:

1. Patient must be 12 years of age or older, **AND**
2. Patient must have baseline PFT's that show moderate to severe asthma with the forced expiratory volume in one second ($FEV_{1.0}$) or peak expiratory flow (PEF) is <80% predicted, and PEF variability of >30%, **AND**
3. Patient must not weigh more than 150 kg, **AND**
4. Patient must be compliant with two existing therapies and have followed the National Heart, Lung and Blood Institute (NHLBI) guidelines for asthma treatment:
   a. Three months of treatment on inhaled steroids■ and long acting beta agonists• or leukotriene inhibitors.▲ **AND**
5. Patient must have significant documented morbidity due to uncontrolled asthma, **AND**
6. Patient must have a baseline serum total IgE between 30 IU/ml and 700 IU/ml, **AND**
7. Patient must have documented evidence of at least one perennial aeroallergen by a skin test (e.g., prick/puncture test) or a blood test (e.g., RAST), **AND**
8. Patient must have:
   - Two or more treatments with oral systemic steroids within the past year with documentation of compliance to the standard controller medications; **OR**
   - At least two documented ER visits in the past year with documentation of compliance to the standard controller medications; **OR**
   - A hospitalization due to asthma with documentation of compliance to the standard controller medications.

■ Inhaled steroids e.g., (Qvar®, Beclovent®, Vanceril®, Vanceril DS®, Pulmicort Turbuhaler®, AeroBid®, AeroBid M®, Flovent®, Azmacort®)

• Long acting beta agonists, e.g., (Serevent®, Foradil®)

▲ Leukotriene inhibitor, e.g., (Singulair®, Accolate®, Zyflo®)

Xolair™ is a medical benefit and should be administered in the physician's office.

After the initial medical criteria for coverage is met for Xolair™, additional treatment with Xolair™ will be covered as long as the patient has a positive response to treatment.

NOTE: Measurement of a baseline serum total IgE level should be done prior to treatment with Omalizumab, and does not need to be monitored during treatment, as the level will be affected by the presence of circulating IgE-anti IgE complexes. Only baseline PFTs, which are performed prior to initiation of Xolair therapy are reviewed for coverage. Repeat PFTs, while recommended by the expert panel, do not need to be submitted.

Xolair™ for the treatment of MODERATE TO SEVERE CHRONIC IDIOPATHIC URTICARIA (CIU) meets Blue Cross and Blue Shield of Alabama's medical policy for coverage when **ALL** of the following criteria are met:

1. Patient must be 12 years of age or older, **AND**
2. Patient has been treated with at least two different high-dose H1-antihistamines (2 – 4 times normal dose daily) unless H1-antihistamine therapy is medically contraindicated, **AND**
3. Patient has been treated with a LTRA in combination with a high-dose H1-antihistamine, unless LTRA therapy is medically contraindicated, **AND**
4. Patient has been treated with an H2-antagonist in combination with a high-dose H1 antihistamine, unless H2-antagonist therapy is medically contraindicated, **AND**
5. Patient has been treated with an anti-inflammatory agent (e.g. dapsone, hydroxychloroquine, sulfasalazine) or an immunosuppressant agent (e.g. cyclosporine, mycophenolate) in combination with a high-dose antihistamine, unless ALL anti-inflammatory and immunosuppressant agents are medically contraindicated, **AND**
6. Patient continues to experience hives associated with itching despite adequate trials (minimum four weeks) of the afore-mentioned stacked therapies (unless otherwise contraindicated).

Xolair™ is a medical benefit and should be administered in the physician's office.

After the initial medical criteria for coverage is met for Xolair™, additional treatment with Xolair™ will be covered as long as the patient has a positive response to treatment.

Xolair™ does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage when used to treat food allergies or hay fever, or when used for asthma patients who continue to smoke.

Effective for dates of service prior to November 8, 2013:

Xolair™ for meets Blue Cross and Blue Shield of Alabama's medical policy for coverage when initially prescribed by a pulmonologist or allergist/immunologist and when **ALL** of the following criteria are met:

1. Patient must be 12 years of age or older.
2. Patient must have baseline PFT's that show moderate to severe asthma with the forced expiratory volume in one second ($FEV_{1.0}$) or peak expiratory flow (PEF) is <80% predicted, and PEF variability of >30%.
3. Patient must not weigh more than 150 kg.
4. Patient must be compliant with two existing therapies and have followed the National Heart, Lung and Blood Institute (NHLBI) guidelines for asthma treatment:
   a. Three months of treatment on inhaled steroids▪ and long acting beta agonists• or leukotriene inhibitors.▲
5. Patient must have significant documented morbidity due to uncontrolled asthma.
6. Patient must have a baseline serum total IgE between 30 IU/ml and 700 IU/ml.

7. Patient must have documented evidence of at least one perennial aeroallergen by a skin test (e.g., prick/puncture test) or a blood test (e.g., RAST).
8. Patient must have:
    - Two or more treatments with oral systemic steroids within the past year with documentation of compliance to the standard controller medications; **OR**
    - At least two documented ER visits in the past year with documentation of compliance to the standard controller medications; **OR**
    - A hospitalization due to asthma with documentation of compliance to the standard controller medications.

■ Inhaled steroids e.g., (Qvar®, Beclovent®, Vanceril®, Vanceril DS®, Pulmicort Turbuhaler®, AeroBid®, AeroBid M®, Flovent®, Azmacort®)

• Long acting beta agonists, e.g., (Serevent®, Foradil®)

▲ Leukotriene inhibitor, e.g., (Singulair®, Accolate®, Zyflo®)

Xolair™ is a medical benefit and should be administered in the physician's office.

After the initial medical criteria for coverage is met for Xolair™, additional treatment with Xolair™ will be covered as long as the patient has a positive response to treatment.

Xolair™ does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage when used to treat food allergies or hay fever, or when used for asthma patients who continue to smoke.

NOTE: Measurement of a baseline serum total IgE level should be done prior to treatment with Omalizumab, and does not need to be monitored during treatment, as the level will be affected by the presence of circulating IgE-anti IgE complexes. Only baseline PFTs, which are performed prior to initiation of Xolair therapy are reviewed for coverage. Repeat PFTs, while recommended by the expert panel, do not need to be submitted.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

In 1999, it was reported that 26.7 million people had been diagnosed with asthma. The Center for Disease Control and Prevention reported that asthma accounted for 12.7 billion dollars in cost in 1998; 4,487 deaths in 2,000 and 400,000-500,000 hospitalizations annually. The cost of asthma treatment is closely related to the level of severity of the disease. Genentech has reported that it expects a patient population of 500,000 patients for the Xolair™ product.

The safety and efficacy of Xolair™ were evaluated in three randomized, double blind, multicenter trials. The trials enrolled individuals 12 to 76 years of age who had moderate to severe persistent asthma based on the National Heart, Lung and Blood Institute (NHLBI) criteria for at least one year. These individuals also had to have positive skin test reaction to perennial aeroallergen. In initial screening, the patients in studies one and two had a forced expiratory volume in one second ($FEV_{1.0}$) between 40 to 80% predicted while in study three there were no restrictions placed on screening $FEV_{1.0}$. All patients had an $FEV_{1.0}$ improvement of at least 12% following beta agonist administration. All patients were symptomatic and were being treated with inhaled corticosteroids and short acting beta agonists. In the third study, long acting beta agonists were prescribed. The patients in study three were receiving at least 1,000 ug/day of Fluticasone Propionate and a subset was also receiving oral corticosteroids. Patients receiving other concomitant controlling medications were excluded and initiation of additional controlling medications while on the study was prohibited. Patients who were currently smoking were also excluded from the study.

Each data set was comprised of a run-in period to achieve a stable conversion to a common inhaled corticosteroid followed by randomization to Xolair™ or placebo. In the third study, patients were stratified by use of the inhaled corticosteroid only or inhaled corticosteroid with common use of oral steroids. Patients received Xolair™ for 16 weeks with an unchanged corticosteroid dose unless an acute exacerbation necessitated an increase. Patients then entered an inhaled corticosteroid reduction phase of 12 weeks in studies one and two and 16 weeks in study three during which the inhaled corticosteroid or oral steroid reduction was attempted in a step-wise manner.

All of the patients were required to have a baseline IgE between 30-700 IU/ml and body weight no more than 150 kg. Patients were treated according to the dosing table to administer at least 0.016 mg/kg/IU of Xolair™ or a matching volume of placebo over a four-week period. The maximum Xolair™ dose per four weeks was 750 mg. Patients were to receive no more than 300 mg within the four-week period and were treated by administering half the total dosage every two weeks. In all three studies an exacerbation was defined as a worsening of asthma that required treatment of systemic corticosteroids or a doubling of the baseline inhaled corticosteroid dose. The result of the studies showed that in study one and two the number of exacerbations per patient was reduced for individuals treated with Xolair™ compared with placebo. In study three, the number of exacerbations in patients treated with Xolair™ was similar to that in placebo treated patients. The absence of an observed treatment effect in study three may be related to the differences in patient population as compared with studies one and two. In all three studies, most exacerbations were managed in the outpatient setting. The majority was treated with systemic steroids. Hospitalization rates were not significantly different between Xolair™ and placebo treated patients, however the overall hospitalization rate was very small. In all three of the

studies the reduction of asthma exacerbation was not observed in the Xolair™ treated patients who had an FEV1 > 80% at the time of randomization. Reductions in exacerbations were not seen in patients who required oral steroids as maintenance therapy. Serious adverse reactions occurring in the clinical studies were malignancies (0.5% in Xolair™ vs. 0.2% in placebo). Anaphylaxis was rare (<0.1%). Patients should be observed after injections of Xolair™ and medications for the treatment of severe hypersensitivity reaction including anaphylaxis should be available.

Xolair™ treatment is generally well tolerated. The most frequent adverse events include injection site reaction (45%), viral infection (23%), upper respiratory tract infection (20%), sinusitis (16%), headache (15%), and pharyngitis (11%). These events were observed at similar rates in Xolair™ treated patients as well as the control group. Typically, the patients who meet the criteria for Xolair™ administration should be followed by an allergist/immunologist or pulmonologist due to the severity of the asthma.

The National Heart, Lung, and Blood Institute and the National Asthma Education and Prevention Program classify severe persistent and moderate persistent based on the chart below:

Disease Severity Classification Scheme Recommended in Current Guidelines					
	Symptoms	**Nighttime Symptoms**	**Lung Function**	**Long-Term-Control Medications**	**Quick-Relief Medications**
Step 4 Severe persistent	• Continual • Limited physical activity • Frequent exacerbations	• Frequent	• $FEV_{1.0}$ or PEF ≤ 60% predicted • PEF variability > 30%	*Preferred treatment:* • High-dose inhaled corticosteroids *and* • Long-acting inhaled $beta_2$ agonists *and (if needed*) • Corticosteroid tablets or syrup long-term	• Short-acting $beta_2$ agonist (two to four puffs as needed) • Intensity of treatment depends on severity • Use of quick-relief more than two times per week might indicate need to step up long-term control therapy
Step 3 Moderate persistent	• Daily • Daily use of inhaled short-acting beta2 agonists • Exacerbations affect activity levels • Exacerbations occur one or more times a week; can last several days	• > One time per week	• $FEV_{1.0}$ or PEF > 60%-< 80% predicted • PEF variability > 30%	*Preferred treatment:* • Low-to-medium dose inhaled corticosteroids *and* • Long-acting, inhaled $beta_2$ agonists • Alternative treatment: • Increase inhaled corticosteroids to a medium dose and add long-acting inhaled $beta_2$ agonists *or* • Low- to medium-dose inhaled corticosteroids and	• Short-acting $beta_2$ agonist (two to four puffs as needed) • Intensity of treatment depends on severity • Use of quick-relief more than two times per week might indicate need to step up long-term control therapy

				either a leukotriene modifier or theophylline to serum concentration of 5-15 mcg/ml	

On February 21, 2007, the U.S. Food and Drug Administration (FDA) announced that it has requested Genentech, Inc., add a black box warning to the product label for omalizumab, marketing as Xolair. The FDA has received new reports of serious and life-threatening allergic reactions (anaphylaxis) in patients after treatment with Xolair. Usually these reactions occur within two hours of receiving Xolair subcutaneous injection. However, these new reports include patients who had delayed anaphylaxis, with onset two to 24 hours or even longer, after receiving Xolair 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. The signs and symptoms of anaphylaxis in these reported patients include bronchospasm, hypotension, syncope, urticaria, and angioedema of the throat or tongue.

Based on reports from approximately 39,500 patients, anaphylaxis following Xolair treatment occurred in at least 0.1% of treated people. Health-care professionals who administer Xolair should be prepared to manage life-threatening anaphylaxis and should observe their Xolair-treated patients for at least two hours after Xolair is given. Patients under treatment with Xolair should be fully informed about the signs and symptoms of anaphylaxis, their chance of developing delayed anaphylaxis following Xolair treatment, and how to treat it when it occurs. Patients should carry medical contact information because delayed anaphylaxis may occur. Patients should also be prepared to begin treatment, such as having an epinephrine auto-injection and being trained in when and how to use it.

The FDA has requested that the Xolair black box warning requirements include the following:

1. Anaphylaxis can occur in patients that have previously not had bad reactions to Xolair.
2. Anaphylaxis can occur up to 24 hours after the Xolair injection is administered.
3. Doctors should observe patients for at least two hours after the drug is administered and be prepared to manage a potentially life-threatening allergic reaction.
4. Patients given Xolair should be able to manage an anaphylactic reaction themselves in an emergency.

The National Heart, Lung and Blood Institute and the National Asthma Education and Prevention Program published an “Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma” in 2007. Some of the new recommendations, as they pertain to Omalizumab, are summarized here.

The expert panel recommended that Omalizumab may be considered as adjunctive therapy in Step 5 or 6 care for patients who have allergies and severe persistent asthma that is inadequately controlled with the combination of high-dose ICS and LABA. The vast majority of patients in clinical trials of Omalizumab had moderate-or-severe persistent asthma incompletely controlled

with ICS; all had atopy and IgE ≥ 30 IU/ml. Adding Omalizumab to ICS therapy generally produced a significant reduction in asthma exacerbations, but not always. Omalizumab, added to ICS, was associated with a small but significant improvement in lung function. In two trials, in patients who had severe persistent asthma inadequately controlled on ICS plus LABAs, Omalizumab reduced asthma exacerbations and ED visits. Omalizumab also appears to have a modest steroid-sparing effect. It has not been compared in clinical trials to the other adjunctive therapies for moderate persistent asthma (LABAs, leukotriene modifiers, and theophylline), all of which improve outcomes and allow reduction of ICS dose. Omalizumab is the only adjunctive therapy, however, to demonstrate added efficacy to high-dose ICS plus LABA in patients who have severe persistent allergic asthma. In studies of patients who have severe persistent asthma, Omalizumab resulted in clinically relevant improvements in quality-of-life scores in significantly more patients (60%) than did placebo (43%).

The expert panel outlined the stepwise approach for managing asthma in patients ≥ 12 years and adults. The steps that relate to Omalizumab are:

> Step 5-Severe persistent asthma: High-dose inhaled corticosteroid and long-acting beta-agonist. Consider Omalizumab for patients who have allergies (supported by level B evidence).
>
> Step 6-Severe persistent asthma: High-dose inhaled corticosteroid, long-acting beta-agonist, and oral corticosteroid. Consider Omalizumab for patients who have allergies.

The expert panel made recommendations concerning Pulmonary Function Tests (spirometry). They recommended that spirometry measurements-FEV1, forced expiratory volume in six seconds (FEV6), FVC, FEV/FVC-before and after the patient inhales a short-acting bronchodilator, should be undertaken for patients in whom the diagnosis of asthma is being considered. The panel noted that in addition to monitoring a patient's symptom history, it is important to assess pulmonary function periodically. The main methods are spirometry and peak flow monitoring. The panel recommended that follow up spirometry may be done after treatment is initiated and symptoms and PEF have stabilized, during a period of prolonged loss of asthma control, and at least every one to two years to assess the maintenance of airway function. Spirometry may be indicated more often than every one to two years, depending on the clinical severity and response to management. The panel also recommended that if peak flow monitoring is performed, the written asthma action plan should use the patient's personal best peak flow as the reference value. Long-term daily peak flow monitoring may be used in patients who have moderate or severe persistent asthma, who have a history of severe exacerbations, who have difficulty perceiving signs of worsening asthma, or who prefer this method.

2011 Update

The FDA is evaluating interim safety findings from an ongoing study of Xolair (omalizumab) that suggests an increased number of cardiovascular and cerebrovascular adverse events in a group of patients using Xolair compared to a group of patients not given the drug (control group).

This ongoing study, titled *Evaluating the Clinical Effectiveness and Long-Term Safety in Patients with Moderate to Severe Asthma* (EXCELS), is an observational study of approximately 5000 Xolair treated patients and a control group of approximately 2500 non-Xolair treated patients. The primary objective of the EXCELS study is to assess the long-term safety profile of Xolair in patients followed for five years. Study patients are 12 years of age and older with moderate to severe persistent asthma and who have a positive skin test or blood test for an aeroallergen.

The interim data, submitted by the manufacturer of Xolair (Genentech), suggests a disproportionate increase in ischemic heart disease, arrhythmias, cardiomyopathy and cardiac failure, pulmonary hypertension, cerebrovascular disorders, and embolic, thrombotic and thrombophlebitic events in patients treated with Xolair compared to the control group of patients not given the drug.

The FDA is not recommending any changes to the prescribing information for Xolair and is not advising patients to stop taking Xolair at this time. Until the evaluation of the EXCELS study is completed, healthcare providers and patients should be aware of the risks and benefits described in the prescribing information, as well as the new information from the ongoing EXCELS study that may suggest a risk of cardiovascular and cerebrovascular adverse events. The Agency will communicate any new findings when its analysis of the interim safety data is complete. The EXCELS study is ongoing and final results are not expected until 2012.

2013 Update

Chonic Idiopathic Urticaria

In 2010, Fonacier et al noted that chronic urticaria is characterized by recurrent pruritic wheals with surrounding erythema for greater than six weeks. It is associated with a significant health care burden and affects patient quality of life. The etiology of chronic urticaria is often difficult to determine. Known etiologies include autoimmune urticaria, physical urticarias (e.g., cold, cholinergic, and delayed pressure urticaria), and idiopathic urticaria. The etiology remains unknown in many patients, leading to a diagnosis of chronic idiopathic urticaria (CIU). The diagnosis of CIU can be challenging to manage due to the chronic nature of the symptoms. Diagnosis requires a detailed patient history and comprehensive physical examination, with additional testing tailored to the patient's history. Effective treatments include anti-histamines, leukotriene receptor antagonists (LKRAs) in combination with anti-histamines, and oral immunomodulatory drugs, including corticosteroids, cyclosporine, dapsone, hydroxychloroquine, and sulfasalazine. Newer therapies include intravenous immunoglobulin and omalizumab (Xolair™).

Several randomized trials have demonstrated the efficacy of omalizumab in CIU not responsive to standard doses of H1 antihistamines. In the largest randomized multicenter trial in 323 patients, ages 12 to 75 years, with persistent moderate-to-severe, Mauer et al (2013) reported that CIU symptoms were treated with three monthly injections of either placebo or omalizumab at doses of 75, 150, or 300 milligrams(mg) subcutaneously, and observed for an additional four months. The primary endpoint was a change in mean weekly itch severity scores (on a scale from 0 to 21, with a minimally important difference of 5) at the end of 12 weeks. Mean itch scores decreased in all groups (-5, -6, -8, -10 points in placebo, 75, 150, and 300 mg groups

respectively); the improvement in scores was statistically significant only in the groups receiving 150 and 300 mg doses. The percentages of subjects with complete resolution of urticarial were 10, 18, 23, and 53, respectively. Following the active treatment stage of the study, patients' symptoms gradually returned during the four months of observation, but did not reach the severity at the start of the study.

A smaller randomized multicenter trial by Mauer et al (2011) included 49 patients with persistent CIU. All subjects had demonstrable IgE autoantibodies to thyroid peroxidase (a test not commercially available), although the role of this antibody in the pathogenensis of CIU, if any, has not been demonstrated. Omalizumab was dosed according to weight and total IgE level, based upon dosing for asthma. The primary endpoint was the change in weekly urticarial activity scores (UAS7) after 24 weeks of therapy. Compared with placebo, omalizumab therapy was associated with a significantly greater reduction in USA7 scores from baseline (-18 versus -8 points) and a significantly higher rate of complete control of CIU (70 versus 5 percent).

The optimal dose and duration of therapy for CIU has not been determined and it is not known if omalizumab has any long-term disease-modifying effects. Comparative studies with other CIU therapies have not yet been performed. However, based on the studies done to date, omalizumab therapy for the treatment of CIU would be reasonable as fourth-line treatment when other treatments have failed or are medically contraindicated.

Summary
There are no other new recommendations or clinical studies in the peer-reviewed literature on the use of Xolair™ to treat asthma. Therefore, this policy remains unchanged with regard to the treatment of moderate- to severe persistent asthma in patients ages 12 and older. This policy is updated to include criteria for use of Xolair™ in the treatment of moderate to severe chronic idiopathic urticaria.

Key Words:
Asthma, omalizumab, IgE, intrinsic asthma, chronic idiopathic urticaria, CIU

Approved by Governing Bodies:
FDA approved June 20, 2003 for the treatment of adults or adolescents (12 years of age or above) with moderate to severe persistent asthma. The specific product labeling outlines the appropriate dosage based on the serum IgE level (before treatment) and weight of the patient.

On February 21, 2007, the FDA requested adding a black box warning label emphasizing that the product may cause anaphylaxis.

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.
PMD physicians are required to submit a predetermination and we strongly recommend non-PMD or other providers to request a predetermination.
The FEP contract does not provide predetermination of benefits. After the initial medical criteria for coverage is met for Xolair™, additional treatment with Xolair™ will be covered as long as the patient has a positive response to treatment.

Coding:

Effective for dates of service on or after January 1, 2005:

J2357 Injection, Omalizumab, 5 mg

References:

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Policy History:

Medical Policy Group, August 2003 **(3)**
Medical Review Committee, September 2003
Medical Policy Administration Committee, August 2003
Available for comment August 11-September 25, 2003
Available for comment October 20-December 3, 2003
Medical Policy Group, October 2004 **(3)**
Medical Policy Administration Committee, October 2004
Available for comment November 2-December 16, 2004
Medical Policy Group, July 2006 **(3)**
Medical Policy Group, March 2007 **(3)**
Medical Policy Administration Committee, March 2007
Medical Policy Group, June 2008 **(3)**
Medical Policy Administration Committee, July 2008
Available for comment July 3-August 18, 2008
Medical Policy Group, August 2011; Updated Key Points & References
Medical Policy Group, September 2013 **(3)**: 2013 Updates to Description, Policy statement, Key Points and References – added coverage criteria for the treatment of moderate to severe chronic idiopathic urticarial (CIU)
Medical Policy Administration Committee, October 2013
Available for comment September 24 through November 7, 2013
Medical Policy Group, June 2014 **(3)**: Editing request – removed "when initially prescribed by a pulmonologist or allergist/immunologist and" from policy statement for chronic idiopathic urticarial (CIU)

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.