



Louisiana

omalizumab (Xolair[®])

Policy # 00222

Original Effective Date: 09/19/2007

Current Effective Date: 09/19/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member's contract/certificate, and
- Medical necessity criteria and guidelines are met.

Asthma

Based on review of available data, the Company may consider omalizumab (Xolair^{®†}) for the management of moderate to severe persistent asthma to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for the use of omalizumab (Xolair) will be considered when all of the following criteria are met:

- Xolair is used for the treatment of moderate persistent or severe persistent asthma (as defined in the current National Heart, Lung, and Blood Institute (NHLBI) Asthma Guidelines) in patients age 6 or greater; and
- Patient has a positive skin test or in vitro reactivity to a perennial aeroallergen; and
- Xolair is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g. reslizumab (Cinqair^{®‡}), mepolizumab (Nucala^{®‡}); AND
- Patient's symptoms are inadequately controlled with combination controller therapy (medium to high doses of inhaled corticosteroids plus long acting beta2-agonists or leukotriene modifiers), or cannot tolerate the medications; and
- Patient has an FEV₁ less than 80% predicted; and
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met. This criterion only applies to the initial treatment request.)*
- Patient has a serum IgE level equal to or greater than 30 IU/ml; and
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met. This criterion only applies to the initial treatment request.)*
- Xolair is ordered by a pulmonologist, allergist, or appropriate specialist
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

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Chronic Idiopathic Urticaria

Based on review of available data, the Company may consider omalizumab (Xolair) for the treatment of chronic idiopathic urticaria to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for the use of omalizumab (Xolair) will be considered when all of the following criteria are met:

- Patient has a diagnosis of Chronic Idiopathic Urticaria (defined by the presence of itchy hives that last for at least 6 weeks, with or without angioedema, and have no apparent external trigger); and
- Patient is 12 years of age or older; and
- Patient remains symptomatic despite at least 6 weeks of treatment with standard therapeutic doses of H1 antihistamine (e.g. cetirizine 10mg, levocetirizine 5mg, fexofenadine 180mg) AND leukotriene modifier combination therapy (e.g. montelukast 10mg)

*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.*

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Asthma

Based on review of available data, the Company considers the use of omalizumab (Xolair) when any of the following patient selection criteria are NOT met to be **investigational**.*

- Xolair is used for the treatment of moderate persistent or severe persistent asthma (as defined in the current NHLBI Asthma Guidelines) in patients age 6 or greater
- Patient has a positive skin test or in vitro reactivity to a perennial aeroallergen
- Xolair is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g. reslizumab (Cinqair), mepolizumab (Nucala)]
- Patient's symptoms are inadequately controlled with combination controller therapy (medium to high doses of inhaled corticosteroids plus long acting beta2-agonists or leukotriene modifiers), or cannot tolerate the medications

Chronic Idiopathic Urticaria

Based on review of available data, the Company considers the use of omalizumab (Xolair) when any of the following patient selection criteria are NOT met to be **investigational**.*

- Patient has a diagnosis of Chronic Idiopathic Urticaria (defined by the presence of itchy hives that last for at least 6 weeks, with or without angioedema, and have no apparent external trigger)
- Patient is 12 years of age or older

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When Services Are Considered Not Medically Necessary

Asthma

Based on review of available data, the Company considers the use of omalizumab (Xolair) when any of the following patient selection criteria are NOT met to be **not medically necessary**:**

- Patient has an FEV₁ less than 80% predicted
- Patient has a serum IgE level equal to or greater than 30 IU/ml
- Xolair is ordered by a pulmonologist, allergist, or appropriate specialist

Chronic Idiopathic Urticaria

Based on review of available data, the Company considers the use of omalizumab (Xolair) when any of the following patient selection criteria are NOT met to be **not medically necessary**:**

- Patient remains symptomatic despite at least 6 weeks of treatment with standard therapeutic doses of H1 antihistamine (e.g. cetirizine 10mg, levocetirizine 5mg, fexofenadine 180mg) AND leukotriene modifier combination therapy (e.g. montelukast 10mg)

Background/Overview

Omalizumab (Xolair) is a recombinant DNA-derived humanized IgG1_k monoclonal antibody that selectively binds to human immunoglobulin E (IgE). Xolair is administered subcutaneously once or twice a month for the asthma indication and the dose is based on total serum IgE concentrations and body weight prior to therapy. Chronic idiopathic urticaria dosing is once monthly and is not weight or serum IgE level dependent.

Asthma

Asthma is a respiratory disorder characterized by increased responsiveness of the trachea and bronchi to various stimuli resulting in the narrowing of the airways, along with mucous secretion. Symptoms vary in severity and intensity and include wheezing, cough and dyspnea. Attacks can be triggered by exercise, allergens, irritants and viral infections. Based on symptoms, the four levels of asthma severity are:

- Mild intermittent (comes and goes)—you have episodes of asthma symptoms twice a week or less, and you are bothered by symptoms at night twice a month or less; between episodes, however, you have no symptoms and your lung function is normal.
- Mild persistent asthma—you have asthma symptoms more than twice a week, but no more than once in a single day. You are bothered by symptoms at night more than twice a month. You may have asthma attacks that affect your activity.
- Moderate persistent asthma—you have asthma symptoms every day, and you are bothered by nighttime symptoms more than once a week. Asthma attacks may affect your activity.
- Severe persistent asthma—you have symptoms throughout the day on most days, and you are bothered by nighttime symptoms often. In severe asthma, your physical activity is likely to be limited.

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Chronic Idiopathic Urticaria

Chronic idiopathic urticaria (CIU) is defined by the presence of itchy hives that last for at least 6 weeks, with or without angioedema, and have no apparent external trigger. Typical treatments for CIU include antihistamines, leukotriene modifiers, and immunomodulatory agents.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Xolair is approved to treat patients 6 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. In 2014, Xolair gained an indication for the treatment of chronic idiopathic urticaria in patients 12 years of age or older who remain symptomatic despite H1 antihistamine treatment. In mid-2016, the indication for asthma was expanded to those 6 years of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Asthma

The initial asthma indication was based on data from three multicenter, randomized, double blind, placebo-controlled studies in over 1,400 patients 12 years of age or older with symptomatic moderate to severe persistent asthma for at least 1 year and a positive skin test reaction to a perennial aeroallergen. In 2 of the 3 studies, treatment with omalizumab was associated with lower incidence of asthma exacerbations compared with placebo; the incidence of asthma exacerbations was similar between omalizumab and placebo in study 3. No reduction in the incidence of asthma exacerbations was observed in patients with a baseline forced expiratory volume in 1 second exceeding 80% or in patients who required oral corticosteroids as maintenance therapy in any of the studies.

The expansion of age for those 6 years to less than 12 years for the asthma indication was based on a randomized, double-blind, placebo controlled, multi-center trial studying pediatric patients aged 6 to less than 12 years of age with moderate to severe asthma. This study was conducted over 52 weeks and was conducted on children who were inadequately controlled despite the use of inhaled corticosteroids with or without controller asthma medications. During the first 24 weeks, the steroid doses remained constant from baseline. The initial 24 week period was then followed with a 28 week period in which the inhaled corticosteroid adjustment was allowed. The primary endpoint was the rate of asthma exacerbations during the 24 week steroid treatment phase. At 24 weeks, the Xolair group had a statistically significantly lower rate of asthma exacerbations (0.45 vs. 0.64) with an estimated rate ratio of 0.69 (95% CI: 0.53, 0.90). The

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Xolair group also had a lower rate of asthma exacerbations compared to placebo over the full 52 week double blind treatment period (0.78 vs. 1.36; rate ratio 0.57; 95% CI: 0.45, 0.72). Other efficacy variables such as nocturnal symptom scores, beta agonist use, and measures of airflow (FEV1) were not statistically significantly different in Xolair treated patients compared to placebo. Another trial lasting 28 weeks demonstrated similar results.

Chronic Idiopathic Urticaria

The safety and efficacy of Xolair for the treatment of CIU was assessed in two placebo-controlled, multiple-dose clinical studies of 24 weeks' duration and 12 weeks' duration. Patients received Xolair 75, 150, or 300 mg or placebo by subcutaneous (SC) injection every 4 weeks in addition to their baseline level of H1 antihistamine therapy for 24 or 12 weeks, followed by a 16-week washout observation period. In both CIU Studies 1 and 2, patients who received Xolair 150 mg or 300 mg had greater decreases from baseline in weekly itch severity scores and weekly hive count scores than placebo at Week 12. The 75-mg dose did not demonstrate consistent evidence of efficacy and is not approved for use.

References

1. American Society of Health-System Pharmacists. AHFS Drug information 2006. Omalizumab 2718-2719.
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4. U.S. FDA. Center for Drug Evaluation and Research (CDER). FDA Labeling Information. Omalizumab (Xolair). 2010.
5. U.S. FDA. CDER. FDA Alert for Omalizumab. Issued February 2007. Updated July 2010.
6. Omalizumab (Xolair), package insert. Genentech. Updated July 2016.
7. Rosenwasser, Lanney. Incorporating Omalizumab into Asthma Treatment Guidelines: Consensus Panel Recommendations. Pharmacy and Therapeutics. June 2003; Vol. 28(6).
8. UpToDate. Chronic Idiopathic Urticaria. Accessed April 2014.

Policy History

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|--------------------------|---|
| Original Effective Date: | 09/19/2007 |
| Current Effective Date: | 09/19/2018 |
| 09/05/2007 | Medical Director review |
| 09/19/2007 | Medical Policy Committee approval. |
| 09/09/2008 | Medical Director review |
| 09/17/2008 | Medical Policy Committee approval. No change to coverage eligibility. Added FDA black box warning to FDA section. |
| 09/03/2009 | Medical Policy Committee approval |
| 09/16/2009 | Medical Policy Implementation Committee approval. No change to coverage eligibility. |
| 09/09/2010 | Medical Policy Committee review |
| 09/15/2010 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 09/01/2011 | Medical Policy Committee review |
| 09/14/2011 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 11/01/2012 | Medical Policy Committee review |
| 11/28/2012 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 02/07/2013 | Medical Policy Committee review |

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- 02/20/2013 Medical Policy Implementation Committee approval. "When services are not covered" section was deleted from policy. Patient selection criteria revised.
 - 05/01/2014 Medical Policy Committee review
 - 05/21/2014 Medical Policy Implementation Committee approval. Added indication for CIU and updated FDA, background, and rationale sections to reflect change.
 - 05/07/2015 Medical Policy Committee review
 - 05/20/2015 Medical Policy Implementation Committee approval. No change to coverage.
 - 05/05/2016 Medical Policy Committee review
 - 05/18/2016 Medical Policy Implementation Committee approval. No change to coverage.
 - 09/08/2016 Medical Policy Committee review
 - 09/21/2016 Medical Policy Implementation Committee approval. Changed the age for the asthma indication to 6 years or older based on updated package insert indication.
 - 01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
 - 09/07/2017 Medical Policy Committee review
 - 09/20/2017 Medical Policy Implementation Committee approval. Clarified that this drug can't be combined with other monoclonal antibodies that typically treat asthma.
 - 09/06/2018 Medical Policy Committee review
 - 09/19/2018 Medical Policy Implementation Committee approval. No change to coverage.
- Next Scheduled Review Date: 09/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|-----------|----------|
| CPT | No codes |
| HCPCS | J2357 |

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| | |
|------------------|-----------------------|
| ICD-10 Diagnosis | All related diagnoses |
|------------------|-----------------------|

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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