MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

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XOLAIR® (omalizumab)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

Description:

Xolair (omalizumab) is a humanized monoclonal antibody produced by recombinant DNA technology that selectively binds to human immunoglobulin E (IgE). It is intended to reduce circulating IgE in individuals with persistent allergic asthma and symptoms that are uncontrolled with inhaled corticosteroids. It is also used in individuals with chronic idiopathic urticaria. Xolair is administered via subcutaneous injection.

Definitions:

Perennial:
Continuing through the entire year.

XOLAIR (omalizumab) (cont.)

Criteria:

Allergic Asthma:

- FDA-approved dosage of Xolair for allergic asthma is considered ***medically necessary*** for non-pregnant, non-nursing individuals 12 years of age or older***** with documentation of **ALL** of the following:

  1. Moderate to severe persistent allergic (e.g., relevant perennial allergens, dust mites, cockroach, cat, dog) asthma
  2. Positive skin test **or** in vitro reactivity to a perennial aeroallergen
  3. Symptoms inadequately controlled with high-dose inhaled corticosteroids (e.g., Pulmicort®, QVAR®, Flovent®, Asmanex®) **and** long-acting beta-agonists (e.g., Serevent®) **or** combination products (e.g., Advair®, Symbicort®)
  4. Body weight not less than 30 kg and not greater than 150 kg
  5. Baseline serum IgE levels not less than 30 IU/ml AND not greater than 700 IU/ml
  6. Dosage calculated according to dosing tables ** provided in the full prescribing information for Xolair******* and should be adjusted for significant changes in body weight
  7. The need for continued therapy should be periodically (at least yearly) reviewed by the prescribing clinician based upon the individual's disease severity and level of asthma control
  8. Xolair infusion will be administered in a controlled health care setting (i.e., physician's office, infusion center) that can provide emergency medical treatment due to the risk of anaphylaxis

* The safety and effectiveness of Xolair in pediatric patients below the age of 12 have not been established.

****** See dosing tables in Resources section.

******* The pivotal clinical trials that established the safety and efficacy of Xolair in asthma excluded patients with baseline serum IgE levels lower than 30 IU/ml or greater than 700 IU/ml and body weight greater than 150 kg (Busse et al. 2001; Soler et al. 2001). Although protocol violations led to the treatment of patients with baseline serum IgE levels and body weight outside the recommended dosing range and inclusion in the overall efficacy analyses, their small numbers were inadequate for meaningful subgroup analysis. As such, the safety and efficacy of doses less than 150 mg or greater than 750 mg per 4-week interval for the treatment of asthma, to accommodate either a body weight or baseline serum IgE level outside the recommended range, have not been established. (Deperi, C., Jan. 30, 2004).

XOLAIR (omalizumab) (cont.)

Criteria: (cont.)

Chronic Idiopathic Urticaria:

See Resources section for FDA-approved dosage.

- FDA-approved dosage of Xolair for chronic idiopathic urticaria is considered ***medically necessary*** with documentation of **ALL** of the following:

  1. Individual is 12 years of age and older
  2. Symptoms despite H1 antihistamine treatment
  3. Dosage is not greater than the FDA approved dosing for the labeled indication (refer to Resource section)

All Other Indications:

- Xolair for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

Resources:

1. American Academy of Allergy Asthma and Immunology. National Asthma Education and Prevention Program. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma Update on Selected Topics, 2002. *J Allergy Clin Immunol.* 2002 Nov;110(5 Suppl):S141-219

2. Berger W, Gupta N, McAlary M, Fowler-Taylor, A. Evaluation of long-term safety of the anti-IgE antibody, omalizumab, in children with allergic asthma. *Ann Allergy Asthma Immunol.* 2003 Aug 2003;91(2):182-188

3. Coffey MJ, Wilfond B, Ross LF. Ethical assessment of clinical asthma trials including children subjects. *Pediatrics.* 2004 Jan 2004;113(1 Pt 1):87-94

4. Drug Facts & Comparisons. Omalizumab. 2003

5. External Consultant Review. Allergy/Immunology. 02/09/2004

XOLAIR (omalizumab) (cont.)

Resources: (cont.)

8. Genentech I, Schmidt E, PharmD, Deperi C, PharmD. Letter: Asthma in children less than 12 years of age. 02/22/2006 2006

9. Genentech Inc., C. Deperi, PharmD. Letter: Baseline IgE levels or weights outside range. 01/30/2004

10. Genentech Inc., P. Maheshwari, PharmD, C. Deperi, PharmD. Letter: Asthma in children less than 12 years old. 10/03/2005

11. Goldsobel, A. Supplement Article: Evaluation of long-term safety of the anti-IgE antibody, omalizumab, in children with allergic asthma. *Pediatrics.* 08/2004 2004;114(2):548-549

12. Lemanske R, Nayak A, McAlary M, Everhard F, Fowler-Taylor A, Gupta N. Omalizumab improves asthma-related quality of life in children with allergic asthma. *Pediatrics.* 11/2002 2002;110(5):e55

13. Milgrom H, Berger W, Nayak A, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). *Pediatrics.* 2001 Aug 2001;108(2):E36

14. National Heart, Lung, Blood Institute. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. *National Asthma Education and Prevention Program.* 2007

15. Rosenwasser L, Nash D. Incorporating omalizumab into asthma treatment guidelines: consensus panel recommendations. *P & T.* 06/2003 2003;28(6):400-410

16. Silkoff P, Romero F, Gupta N, Townley R, Milgrom H. Exhaled nitric oxide in children with asthma receiving xolair (omalizumab), a monoclonal anti-immunoglobulin E antibody. *Pediatrics.* 04/2004 2004;113(4):e308-e312

XOLAIR (omalizumab) (cont.)

Resources: (cont.)

FDA Product Approval Information for Xolair (omalizumab):

- FDA-approved indication: For 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. For FDA-approved dosage for this indication, refer to dosing tables on next page.

  For adults and adolescents (12 years of age and above) with chronic idiopathic urticaria who remain symptomatic despite H1 antihistamine treatment. FDA-approved dosage for this indication is 150 or 300 mg SC every 4 weeks.

  Important Limitations of Use:
  - Not indicated for other allergic conditions or other forms of urticaria
  - Not indicated for acute bronchospasm or status asthmaticus
  - Not indicated for pediatric patients less than 12 years of age

XOLAIR (omalizumab) (cont.)

Resources: (cont.)

Table 1
ADMINISTRATION EVERY 4 WEEKS
Xolair Doses (milligrams) Administered by Subcutaneous Injection Every 4 Weeks for Adults and Adolescents (12 Years of Age and Older) With Asthma

Pre-treatment Serum IgE (IU/ml)	Body Weight (kg)			
	30-60	> 60-70	> 70-90	> 90-150
≥ 30-100	150	150	150	300
> 100-200	300	300	300	
> 200-300	300			
> 300-400				
> 400-500	**SEE TABLE 2**			
> 500-600				

Table 2
ADMINISTRATION EVERY 2 WEEKS
Xolair Doses (milligrams) Administered by Subcutaneous Injection Every 2 Weeks for Adults and Adolescents (12 Years of Age and Older) With Asthma

Pre-treatment Serum IgE (IU/ml)	Body Weight (kg)			
	30-60	> 60-70	> 70-90	> 90-150
≥ 30-100				
> 100-200	**SEE TABLE 1**			225
> 200-300		225	225	300
> 300-400	225	225	300	
> 400-500	300	300	375	
> 500-600	300	375	**DO NOT DOSE**	
> 600-700	375			

Tables source: FDA Prescribing Information, 2014