Omalizumab (Xolair®) Criteria for Non-Formulary Use

VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel

The following recommendations are dynamic and will be revised, as new clinical data become available. These criteria are not intended to interfere with clinical judgment. Rather, they are intended to assist practitioners in providing cost effective, consistent, high quality care.

Omalizumab is a recombinant humanized monoclonal anti-IgE antibody that selectively binds to the Cε3 domain of IgE, which inhibits free IgE from binding to the mast cell FcεR1 receptor thereby preventing activation and subsequent release of cellular mediators.

Given the paucity of long-term safety and efficacy data, an invasive route of administration and a high cost, omalizumab cannot be considered a substitute for accepted first line treatment (inhaled steroid AND long-acting beta-agonist) for the long-term control of persistent asthma. To date, no clinical trial has evaluated the effectiveness of omalizumab in patients already receiving optimal therapy. Until such data are available, the use of omalizumab in allergic asthma is unclear and therefore its use cannot be generally recommended. In asthmatics that remain poorly controlled despite optimal first/second line therapy, providers may consider a trial of omalizumab. In addition to well-defined goals*, the entry criteria into such a therapeutic trial must include all of the following:

Potential Candidates for Non-formulary Use of Omalizumab

ALL of the following must be met

- Patient has moderate or severe persistent asthma as defined by a) symptoms and b) PEF or FEV1 criteria per the National Asthma Education and Prevention Program (NAEPP) Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma-Update on selected Topics NIH publication No. 02-5076; July 2002. http://www.nhlbi.nih.gov/guidelines/asthma/index.htm
- Patient is symptomatic despite having received optimal (preferred) therapy for their asthma per the NAEPP guideline (i.e. are on both inhaled corticosteroids and long-acting beta2-agonists).
- Patient is compliant with their medications as evidenced by a review of compliance with refilling prescriptions during the last 12 months.
- Patient should be nonsmoking and if not, actively receiving smoking cessation treatment
- Serum IgE 30-700 IU/ml.
- Positive skin tests or *in vitro* reactivity to common aeroallergen (e.g. dust mites, pet dander, and cockroach).
- Repeated use of health care services (urgent clinic visit, ER visit, urgent phone call management, or hospitalization) in the last 12 months due to asthma

  OR

  Oral steroid dependent (must have documentation that previous attempts at dosage reduction or discontinuation lead to exacerbation)**

*All new therapies should be evaluated for efficacy and discontinued if not useful. Goal should be the objective improvement in selected markers of asthma control, such as symptoms severity, frequency of rescue treatments, oral steroid requirements, frequency of urgent outpatient visits and/or hospitalization. Effectiveness of therapy should be evaluated after 6 months.

** A small subgroup analysis of patients receiving oral steroids resulted in no difference in outcomes between omalizumab and placebo. Larger studies in oral steroid dependent asthmatics are needed; however, due to the serious adverse effects associated with chronic oral steroid use, a trial of omalizumab may be considered.

SAFETY ISSUES

It is unknown if IgE plays a surveillance role in cancer prevention and whether blocking IgE is associated with an increase in cancer incidence. In the clinical trials, the incidence of new or recurrent cancer with omalizumab and placebo was 0.5% and 0.2% respectively. The majority of these patients were observed for less than 1year. When expressed as 1000 patient-years of exposure the event rate was 6.3 and 3.3 respectively. The sponsor is planning long-term trials to determine whether there is a relationship between omalizumab treatment and cancer.

The safety of omalizumab use in those traveling to endemic parasitic regions is unknown. There is an ongoing study in Brazil evaluating omalizumab in patients who have intestinal helminthic exposure. In the clinical trials, no patient developed anti-omalizumab antibodies and there was no evidence of immune complex disease.

DOSAGE

Omalizumab is administered subcutaneously. Dose and dosing frequency is based on serum total IgE level measured before the start of treatment and body weight (Table 6). No more than 150mg is injected at a single site. Doses > 150mg are to be divided among more than 1 injection site. Dosage adjustments may be made based on changes in body weight. Repeat IgE levels cannot be used to adjust dose as total levels which measure both the omalizumab:IgE complex and free IgE are elevated. Total monthly doses greater than 750mg have not been studied.

Omalizumab dosing

Pre-tx serum IgE (IU/mL)	Body weight (kg)				Dosing frequency
	30-60	>60-70	>70-90	>90-150	
30-100	150mg	150mg	150mg	300mg	Q4 weeks
>100-200	300mg	300mg	300mg	225mg	Q2 weeks
>200-300	300mg	225mg	225mg	300mg	
>300-400	225mg	225mg	300mg	Do not dose	
>400-500	300mg	300mg	375mg		
>500-600	300mg	375mg	Do not dose		
>600-700	375mg	Do not dose			

PREPARATION FOR ADMINISTRATION

Omalizumab is for single use only and contains no preservatives. The solution should be used for SC administration within 8 hours following reconstitution when stored in the vial at 2-8°C (36-46°F), or within 4 hours of reconstitution when stored at room temperature.

The lyophilized product takes 15-20 minutes to dissolve. The fully reconstituted product will appear clear or slightly opalescent and may have a few small bubbles or foam around the edge of the vial. The reconstituted product is somewhat viscous; in order to obtain the full 1.2 mL dose, ALL OF THE PRODUCT MUST BE WITHDRAWN from the vial before expelling any air or excess solution from the syringe.

A vial delivers 1.2 mL (150 mg) of omalizumab. For a 75 mg dose, draw up 0.6 mL into the syringe and discard the remaining product.

COST
The FSS cost for each 150mg vial is $323.29.

Dose	# of vials/ month	Cost/year
150mg	1	$3879.49
300mg	2	$7758.96
450mg (administered as 225mg twice monthly)*	4	$15, 517.92
600mg (administered as 300mg twice monthly	4	$15, 517.92
750mg (administered as 375mg twice monthly*	6	$23,276.88

*For a 75mg dose, withdraw 0.6ml and discard remaining product