



NATIONAL PBM BULLETIN

July 10, 2007

DEPARTMENT OF VETERANS AFFAIRS (VA) VETERANS HEALTH ADMINISTRATION (VHA)
NATIONAL PHARMACY BENEFITS MANAGEMENT STRATEGIC HEALTHCARE GROUP (PBM),
MEDICAL ADVISORY PANEL (MAP), AND
CENTER FOR MEDICATION SAFETY (VA MedSAFE)

Omalizumab (Xolair®) and Anaphylactic Reactions

- I. **ISSUE** – Serious and life-threatening allergic reactions (anaphylaxis) have occurred in patients immediately as well as with delayed onset after receiving treatment with Xolair® (omalizumab).
- II. **BACKGROUND** – The Food and Drug Administration (FDA) has reported 124 cases (estimated number of patients treated during this period is 57,300) of anaphylaxis between June 2003 and December 2006. Signs and symptoms reported include bronchospasm, hypotension, syncope, urticaria, angioedema of the throat or tongue, dyspnea, cough, chest tightness, cutaneous angioedema, and generalized pruritis.
- Important considerations include:
- **Onset can be delayed after administration.** Reactions developing within 30 minutes of administration occurred in 35% of cases, within 30-60 minutes in 16% of cases, and within 60-90 minutes in 8%. Reactions occurring after 2 ->24 hours of administration occurred in 32% of cases. Time of occurrence was unknown for 9% of cases.
 - **Anaphylaxis can occur after any dose even if previous doses were well tolerated.** 39% of cases occurred after the first dose, 19% of cases after the 2nd dose, 10% after the 3rd dose, and the remainder with subsequent doses. Anaphylaxis has occurred beyond one year after beginning regular treatment with omalizumab.
 - 15% of cases resulted in hospitalization.
 - 24% of patients had a prior history of anaphylaxis unrelated to omalizumab.
 - Among 23 patients who developed anaphylaxis and were rechallenged with omalizumab, 18 had a recurrence of similar symptoms.
- III. **DISCUSSION** – Omalizumab was approved for use in 2003 for moderate to severe persistent asthma in patients \geq 12 years of age with a positive skin test to perennial allergens that have had suboptimal control with inhaled corticosteroids. Anaphylaxis became a safety concern during clinical trials for omalizumab and persisted post-market, resulting in the FDA's request for revised labeling to highlight anaphylaxis in a boxed warning and to strengthen the existing warning. As of the end of 3rd quarter 2007, 152 patients were receiving omalizumab in the VA.
- IV. **RECOMMENDATIONS** - *PBM and VAMedSAFE have the same recommendations as the FDA Safety Notice.*
At present, the FDA MedWatch Safety notice recommends the following (from the second bullet point onward):
- Primary care and emergency room physicians should be aware of delayed-onset anaphylaxis that may occur after receiving omalizumab (any dose).
 - Patients who have had a prior allergic reaction to omalizumab should not receive future doses.
 - Healthcare professionals should be prepared to manage life-threatening anaphylaxis.
 - Give patients the omalizumab Medication Guide and instruct them to read it before each omalizumab prescription.
 - Observe patient for at least 2 hours after receiving omalizumab.
 - Educate patients on signs and symptoms of severe hypersensitivity and anaphylaxis.
 - Patients should carry and know how to initiate emergency self-treatment for anaphylaxis.
 - If a severe hypersensitivity reaction occurs, omalizumab should be discontinued.
 - Report adverse events to VHA's Adverse Drug Event Reporting Program and/or FDA's MedWatch program.