



Information for Healthcare Professionals (Please see Updated Healthcare Professional Sheet)

Omalizumab (for Subcutaneous Use) (marketed as Xolair)

FDA ALERT [2/2007]: FDA has received new reports of serious and life-threatening allergic reactions (anaphylaxis) in patients after treatment with Xolair (omalizumab). Usually these reactions occur within two hours of receiving a 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 symptoms and signs 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 (see “Information for Patients” below).

Xolair is approved to treat 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. The Xolair label includes warnings about the chance of anaphylaxis after treatment with Xolair.

This information reflects FDA’s current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program and complete a form on line at <http://www.fda.gov/medwatch/report/hcp.htm> or report by fax to 1-800-FDA-0178, by mail using the postage-paid address form provided on line, or by telephone to 1-800-FDA-1088.

Recommendations and Considerations for Health Care Professionals administering Xolair:

- Be prepared to identify and treat anaphylaxis after Xolair treatment:
 - Know anaphylaxis can occur after any dose of Xolair, even if past doses were well tolerated
 - Provide direct medical supervision when patients are given Xolair
 - Observe patients for at least two hours following each Xolair injection
 - Have trained personnel, medications, and equipment for the treatment of life-threatening anaphylaxis available when administering Xolair. Medical personnel administering Xolair should be prepared to recognize and treat anaphylaxis.



Report serious adverse events to FDA’s MedWatch reporting system by completing a form on line at <http://www.fda.gov/medwatch/report/hcp.htm>, by faxing (1-800-FDA-0178), by mail using the postage-paid address form provided on line (HF-2, 5600 Fishers Lane, Rockville, MD 20853-9787), or by telephone (1-800-FDA-1088).

*Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@cder.fda.gov*



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- Inform patients receiving Xolair treatment of their chance of developing anaphylaxis (including anaphylaxis delayed for 24 hours or more following Xolair treatment) and how to treat it if it occurs. The “Information for the patient” section below provides more detail.
- Discontinue Xolair in patients who experience a severe hypersensitivity reaction
- Report patients who have adverse events including anaphylaxis or hypersensitivity to the FDA’s MedWatch program (see reporting information at the bottom of this page)
- Periodically reassess the need for continued Xolair therapy based upon the patient’s disease severity and level of asthma control

Information for the patient:

Physicians who are prescribing Xolair should discuss the following issues with their patients.

- Because of the chance of anaphylaxis with Xolair, patients should receive Xolair treatment in a doctor’s office and be observed for at least two hours after each treatment
- Anaphylaxis can be serious and life-threatening. Symptoms of anaphylaxis include:
 - Wheezing, cough, chest tightness, or increased trouble with breathing
 - Dizziness, fainting, rapid or weak heartbeat
 - Swelling in the mouth and throat or difficulty swallowing
 - Flushing, itching, hives, or a sensation of warmth
 - Vomiting, diarrhea, or abdominal cramping
- Anaphylaxis can occur with the first dose or after any dose of Xolair
- Anaphylaxis can begin 24 hours or more after Xolair treatment
- Because delayed anaphylaxis occurs after Xolair treatment, patients receiving Xolair treatment should carry medical contact information and be fully prepared to begin treatment for anaphylaxis
- Treatment for anaphylaxis includes:
 - Having an epinephrine auto-injector and being trained in when and how to use it; and
 - Seeking medical attention immediately when symptoms as described above appear
- Patients receiving Xolair should not decrease the dose of, or stop taking, any other asthma medications unless otherwise instructed by their physician
- Patients may not see immediate improvement in their asthma after beginning Xolair therapy



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Background Information and Data

Clinical trial experience

Three cases of anaphylaxis were identified among the 3,507 subjects exposed to Xolair in premarketing clinical trials. Reports of anaphylaxis were based on investigator judgment in relationship to the study drug. In addition to these three cases, there were two cases of dyspnea and/or wheezing with urticaria that were not reported as anaphylaxis, but meet the diagnostic criteria for anaphylaxis that were used to define the postmarketing cases (see below). One of these patients developed localized urticaria, dyspnea, coughing, and wheezing after receiving the first dose of Xolair. The second patient experienced urticaria, dyspnea, and hot flushes the day after receiving the third dose of Xolair.

Postmarketing Cases

Based on a review of 48 case reports submitted to the FDA from June 2003 to December 2005 and an estimated exposure of about 39,500 patients, the frequency of anaphylaxis attributed to Xolair use was estimated to be at least 0.1% of treated patients. The case definition of anaphylaxis used for this review included either skin or mucosal tissue involvement with airway compromise, or reduced blood pressure with or without associated symptoms; and a temporal relationship with Xolair administration with no other identifiable cause.

Symptoms and signs of anaphylaxis in these reported cases included bronchospasm, hypotension, syncope, urticaria, angioedema of the throat or tongue, dyspnea, cough, chest tightness, cutaneous angioedema, and generalized pruritus. Some patients required oxygen and parenteral medications. Pulmonary involvement, including bronchospasm, dyspnea, cough, or chest tightness, was reported in 96% of the cases. Hypotension or syncope was reported in 13% of cases. Fifteen percent of these patients required hospitalization. While most cases of anaphylaxis (71%) occurred within the first 2 hours after Xolair administration, some (13%) occurred later, up to about 24 hours after administration. Anaphylaxis occurred after the first dose of Xolair in 40% of cases, and after repeat administration in 56% of cases. In some cases, anaphylaxis was reported after two years of chronic treatment. Five patients who experienced anaphylaxis were rechallenged with Xolair; all had a recurrence of similar symptoms of anaphylaxis.



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