

## FDA Approves Label Changes for Asthma drug Xolair (omalizumab) Due to Adverse Events

On September 26 the FDA released a drug safety communication concerning the asthma drug Xolair (omalizumab). A label change was approved including describing slightly higher risk of heart/brain adverse events and the risk of various cancers.

FDA approved Xolair in 2003 to treat patients 12 years and older with moderate to severe persistent asthma who have a positive skin or blood test to year-round allergens in the air and whose symptoms are not well-controlled by inhaled corticosteroids. Xolair is also approved for patients 12 years and older with chronic idiopathic urticaria who continue to have hives that are not controlled by H<sub>1</sub> antihistamine treatment.

A review of a 5 year safety study found a slightly higher rate of heart and brain blood vessel problems in patients being treated with Xolair compared to those patients not treated with Xolair.

The heart and brain blood vessel problems that occurred were: transient ischemic attacks (TIAs), myocardial infarctions (MI), unstable angina, pulmonary hypertension, and emboli in the lungs and veins.

Even though the data suggested a serious safety concern, due to weaknesses in the study design and implementation, the exact increased level of these risks with Xolair is unknown.

To further determine the potential risks associated with Xolair, a combined analysis of 25 randomized double-blind clinical trials comparing Xolair to a placebo was reviewed. There was no increased risk of heart and brain related problems noted in this combined analysis. However, the low number of events, young patient population, and short duration of follow-up prevented any definite conclusions from these studies.

Additionally, although some previous clinical trials have shown slightly higher rates of various cancers in patients treated with Xolair compared with placebo (e.g., breast, non-melanoma skin, prostate, melanoma, and parotid gland?), the 5 year safety study mentioned previously found no difference. Malignant neoplasms were observed in 20 of 4127 (0.5%) XOLAIR-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents ( $\geq 12$  years of age) with asthma and other allergic disorders. No exact determination of an increased cancer risk can be made due to the limitations of the study.

In summary, despite the limitations of the available information to date, information stating that there may be a higher risk of cardiovascular adverse events and the risk of various cancers was added by the FDA to the Adverse Drug Reactions and Warnings & Precautions sections (respectively) of the drug label. Clinicians may want to keep these possible (yet unconfirmed) risks in mind when deciding the best therapeutic regimen for their patients. Continued monitoring of omalizumab is needed to better substantiate the drug's risk of cardiovascular and cancer-related adverse events.

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### References

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