



## Omalizumab

Updated: June 18, 2015.

## OVERVIEW

### Introduction

Omalizumab is a monoclonal antibody to human immunoglobulin E (IgE), which leads to a decrease in IgE binding to mast cells and basophils and a reduction in allergic symptoms of asthma and seasonal rhinitis. Omalizumab therapy has not been associated with serum enzyme elevations during therapy and has yet to be implicated in cases of clinically apparent drug induced liver injury with jaundice.

### Background

Omalizumab (oh" ma liz' ue mab) is a recombinant, human monoclonal antibody to IgE which binds avidly to circulating immunoglobulin E, preventing its attachment to high affinity receptors on mast cells and basophils. This receptor inhibition prevents the release of histamine and other mediators of the allergic immune response, reducing airway inflammation and spasm and alleviating symptoms of asthma and allergic rhinitis. Therapy with omalizumab has been shown to reduce the requirement for inhaled corticosteroids and lower the frequency of exacerbations of asthma and to decrease the severity and symptoms of chronic urticaria of unknown cause. Omalizumab was approved for use in the United States in 2003 for therapy of patients with severe and persistent asthma despite corticosteroid inhalation therapy. The indications were extended in 2014 to include chronic idiopathic urticaria. Omalizumab has been evaluated in patients with seasonal rhinitis, but has yet to be approved for that use. Omalizumab is available in single use vials of 150 mg under the brand name Xolair. The recommended dose is 150 to 300 mg intravenously every 4 weeks or 225 to 375 mg every 2 weeks based upon body weight and IgE levels. Common side effects include injection site reactions, rash, diarrhea, nausea and vomiting and epistaxis. Rarely, omalizumab can cause serious acute anaphylaxis or anaphylactoid reactions (~0.1%) and should be given under close medical supervision.

### Hepatotoxicity

In large clinical trials, omalizumab was not associated with changes in serum aminotransferase levels during therapy, and rates of most adverse reactions were similar in patients who received omalizumab or placebo. There have been no published reports of clinically apparent acute liver injury attributed to omalizumab therapy. Thus, liver injury from omalizumab must be very rare, if it occurs at all.

### Mechanism of Injury

Omalizumab is a human monoclonal antibody and is unlikely to be inherently hepatotoxic. While most recombinant proteins are metabolized by the liver, the metabolism leads largely to small peptides and amino acids which may be reused to synthesize proteins and are unlikely to be toxic or immunogenic. Omalizumab

lowers serum levels of IgE, which seems to have no adverse effects on the liver and does not result in significant immunosuppression.

Drug Class: [Antiasthmatic Agents, Monoclonal Antibodies](#)

## PRODUCT INFORMATION

### REPRESENTATIVE TRADE NAMES

Omalizumab – Xolair®

### DRUG CLASS

Antiasthmatic Agents

### COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

## CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Omalizumab	<a href="#">242138-07-4</a>	Monoclonal Antibody	Not Available

## ANNOTATED BIBLIOGRAPHY

References updated: 18 June 2015

Zimmerman HJ. Drugs used to treat rheumatic and musculoskeletal disease. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 517-54. (

*Expert review of hepatotoxicity published in 1999, well before the availability of most monoclonal antibody therapies).*

Reuben A. Hepatotoxicity of immunosuppressive drugs. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2011, pp. 569-91.

*(Review of hepatotoxicity of immunosuppressive agents; "the biological immuno-suppressants are largely free from hepatotoxicity, with the exception of the TNF alpha antagonists"; omalizumab is not specifically mentioned).*

Barnes PJ. Pulmonary pharmacology. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1031-65.

*(Textbook of pharmacology and therapeutics).*

Milgrom H, Fick RB Jr, Su JQ, Reimann JD, Bush RK, Watrous ML, Metzger WJ. Treatment of allergic asthma with monoclonal anti-IgE antibody. rhuMAB-E25 Study Group. N Engl J Med 1999; 341: 1966-73. PubMed PMID: 10607813.

*(In a controlled trial of omalizumab vs placebo for 20 weeks in 317 patients with asthma, side effects were similar between the two groups; no mention of ALT elevations or hepatotoxicity).*

Casale TB, Condemi J, LaForce C, Nayak A, Rowe M, Watrous M, McAlary M, et al.; Omalizumab Seasonal Allergic Rhinitis Trial Group. Effect of omalizumab on symptoms of seasonal allergic rhinitis: a randomized controlled trial. *JAMA* 2001; 286: 2956-67. PubMed PMID: 11743836.

*(A controlled trial of 3 doses of omalizumab versus placebo in 536 patients with allergic rhinitis reported no difference in adverse events between omalizumab and placebo therapy, and "there were no clinically significant alterations in laboratory values in either group").*

Milgrom H, Berger W, Nayak A, Gupta N, Pollard S, McAlary M, Taylor AF, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody(omalizumab). *Pediatrics* 2001; 108: E36. PubMed PMID: 11483846.

*(Controlled trial of omalizumab versus placebo in 536 patients with asthma for 4 months found similar rates of adverse events in the two groups).*

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; 91: 182-8. PubMed PMID: 12952113.

*(Among 225 children with asthma treated with omalizumab for up to 52 weeks, "There were no clinically significant changes... in laboratory safety tests").*

Omalizumab (Xolair): an anti-IgE antibody for asthma. *Med Lett Drugs Ther* 2003; 45(1163): 67-8. PubMed PMID: 12915804.

*(Concise review of the efficacy and safety of omalizumab shortly after its approval for use in asthma in the US; no mention of ALT elevations or hepatotoxicity).*

Ruffin CG, Busch BE. Omalizumab: a recombinant humanized anti-IgE antibody for allergic asthma. *Am J Health Syst Pharm* 2004; 61: 1449-59. PubMed PMID: 15332692.

*(Overview of the chemistry, mechanisms of action, pharmacology, efficacy and safety of omalizumab as therapy of asthma states that the rate of common adverse effects is similar between omalizumab and placebo treated patients; no mention of ALT elevations or hepatotoxicity).*

Strunk RC, Bloomberg GR. Omalizumab for asthma. *N Engl J Med* 2006; 354: 2689-95. PubMed PMID: 16790701.

*(Review of the mechanism of action of omalizumab in asthma and studies of its efficacy and safety; no mention of ALT elevations or hepatotoxicity).*

Antonicelli L, Stagnozzi G, Giuliodoro S, Abbruzzetti A, Massaccesi C. The safety of omalizumab therapy in a patient with severe persistent allergic asthma and hepatitis C. *Ann Allergy Asthma Immunol* 2009; 103: 269-70. PubMed PMID: 19788028.

*(Analysis of results from a single patient with chronic hepatitis C and severe asthma who received omalizumab for 19 months with a beneficial response and no change in serum ALT or HCV RNA levels).*

Corren J, Casale TB, Lanier B, Buhl R, Holgate S, Jimenez P. Safety and tolerability of omalizumab. *Clin Exp Allergy* 2009; 39: 788-97. PubMed PMID: 19302249.

*(Review of the safety of omalizumab in 7500 patients controlled studies in asthma, allergic rhinitis and related conditions reported that overall and serious adverse event rates were similar between omalizumab and placebo groups, and that "There were no between-treatment-group differences  $\geq 2\%$  in the frequency of shifts from normal to abnormal in liver function tests").*

Hanania NA, Alpan O, Hamilos DL, Condemi JJ, Reyes-Rivera I, Zhu J, Rosen KE, et al. Omalizumab in severe allergic asthma inadequately controlled with standard therapy: a randomized trial. *Ann Intern Med* 2011; 154: 573-82. PubMed PMID: 21536936.

*(Controlled trial of omalizumab versus placebo for 48 weeks in 850 patients with asthma found similar rates of serious adverse events and stated that "no clinically relevant abnormality of laboratory tests was observed").*

Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Giménez-Arnau A, Agarwal S, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med* 2013; 368: 924-35. PubMed PMID: 23432142.

*(Controlled trial of 3 doses of omalizumab versus placebo for 16 weeks in 323 patients with chronic urticaria stated that "the frequency of adverse events were similar across groups"; ALT elevations and hepatotoxicity were not mentioned).*

Drugs for asthma and COPD. *Treat Guidel Med Lett* 2013; 11 (132): 75-86. PubMed PMID: 23896773.

*(Concise summary of guidelines for therapy of asthma mentions that omalizumab is approved for use in severe, persistent asthma; no mention of ALT elevations or hepatotoxicity).*

Tsabouri S, Tseretopoulou X, Priftis K, Ntzani EE. Omalizumab for the treatment of inadequately controlled allergic rhinitis: a systematic review and meta-analysis of randomized clinical trials. *J Allergy Clin Immunol Pract* 2014; 2: 332-340. PubMed PMID: 24811026.

*(Systematic review of 11 controlled trials of omalizumab in 2870 patients with allergic rhinitis found no difference in rates of any adverse event between omalizumab and placebo; no specific discussion of ALT elevations or clinically apparent liver injury).*