

Dear Doctor:

We are pleased to present to you the article, "Effect of Ezetimibe Coadministered With Atorvastatin in 628 Patients With Primary Hypercholesterolemia: A Prospective, Randomized, Double-Blind Trial," by Christie M. Ballantyne et al, for the Ezetimibe Study Group, as published in *Circulation*, May 20, 2003.

The effect of ZETIA<sup>®</sup> (ezetimibe) on cardiovascular morbidity and mortality has not been determined.

**ZETIA, administered alone or in combination with an HMG-CoA reductase inhibitor (statin), is indicated as adjunctive therapy to diet** for the reduction of elevated TOTAL-C, LDL-C, and Apo B in patients with primary (heterozygous familial and nonfamilial) hyperlipidemia when diet alone is not enough.

**Contraindications:** hypersensitivity to any component of this medication.

Statin contraindications apply when used with a statin: active liver disease; unexplained persistent elevations in hepatic transaminase levels. Statins are contraindicated in pregnant and nursing women. Refer to the statin label for details.

When using ZETIA with a statin, also follow the label recommendations for that specific statin.

**Selected Cautionary Information:** When ZETIA was coadministered with a statin, consecutive elevations in hepatic transaminase levels ( $\geq 3 \times$  ULN) were slightly higher (1.3%) than those of statins alone (0.4%). Liver function tests should be performed when ZETIA is added to statin therapy and according to statin recommendations. Should an increase in ALT or AST  $\geq 3 \times$  ULN persist, consider withdrawal of ZETIA and/or the statin.

Patients should be advised to promptly report muscle pain, tenderness, or weakness. Risk for skeletal muscle toxicity increases with higher statin doses, advanced age (>65), hypothyroidism, renal impairment, and depending on the statin used, concomitant use of other drugs. Discontinue drug if myopathy is diagnosed or suspected.

ZETIA is not recommended in patients with moderate to severe hepatic impairment.

The coadministration of ZETIA with fibrates other than fenofibrate is not recommended until use in patients is adequately studied.

Exercise caution when using ZETIA and cyclosporine concomitantly because exposure to both drugs is increased. Cyclosporine concentrations should be monitored in these patients.

ZETIA should be used in pregnant or nursing women only if the benefit outweighs the risk.

In clinical trials, regardless of causality assessment, the most frequent side effects for ZETIA coadministered with a statin vs statin alone included nasopharyngitis (3.7% vs 3.3%), myalgia (3.2% vs 2.7%), upper respiratory tract infection (2.9% vs 2.8%), arthralgia (2.6% vs 2.4%), and diarrhea (2.5% vs 2.2%); for ZETIA administered alone vs placebo: upper respiratory tract infection (4.3% vs 2.5%), diarrhea (4.1% vs 3.7%), arthralgia (3.0% vs 2.2%), sinusitis (2.8% vs 2.2%), and pain in extremity (2.7% vs 2.5%).

**Before prescribing ZETIA, please read the accompanying Prescribing Information.**

For additional copies of the Prescribing Information, call 1-866-637-2501, visit [zetia.com](http://zetia.com), or contact your MSP representative.

Sincerely,



Anastasia G. Daifotis, MD  
Vice President, Global Medical Affairs

Enclosure: Prescribing Information for ZETIA