



Dear Doctor:

We are pleased to present to you the following article: "Efficacy and Safety of the Coadministration of Ezetimibe With Fenofibrate in Patients With Mixed Hyperlipidaemia," by Michel Farnier et al, as published in the *European Heart Journal*, March 2005.

The effects of ZETIA<sup>®</sup> (ezetimibe), either alone or in addition to a statin or fenofibrate, on the risk of cardiovascular morbidity and mortality have not been established.

**ZETIA administered in combination with fenofibrate is indicated as adjunctive therapy to diet** for the reduction of elevated TOTAL-C, LDL-C, Apo B, and non-HDL-C in adult patients with mixed 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.

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.

If cholelithiasis is suspected in a patient receiving ZETIA and fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered.

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 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%).

Incidence rates (95% CI) for clinically important elevations ( $\pm 3 \times$  ULN, consecutive) in hepatic transaminase levels were 4.5% (1.9, 8.8) and 2.7% (1.2, 5.4) for fenofibrate monotherapy (n=188) and ZETIA coadministered with fenofibrate (n=183), respectively, adjusted for treatment exposure.

When ZETIA was coadministered with fenofibrate, incidence rates for cholecystectomy were 0.6% and 1.7% for fenofibrate monotherapy and ZETIA coadministered with fenofibrate, respectively.

**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



Dear Doctor:

We are pleased to present to you the following article: "Safety and Efficacy of Long-Term Co-Administration of Fenofibrate and Ezetimibe in Patients With Mixed Hyperlipidemia" by James M. McKenney et al, as published in the *Journal of the American College of Cardiology*, April 18, 2006.

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