LETTER TO THE EDITOR

Safety and Tolerability of Ezetimibe

November 28, 2003

Dear Editor,


The CJCP article notes in its Tolerability and Safety section, that "The clinical studies of ezetimibe alone or in combination have demonstrated adverse event profiles that are very similar to placebo. No significant excess in liver enzymes, creatine kinase or other laboratory parameters were observed in the ezetimibe monotherapy studies. In addition, no increase in adverse gastrointestinal events was observed. In pooled combination studies of ezetimibe and statin, the incidence of consecutive elevations in serum transaminases was 1.3% in the combination group compared with 0.4% in the statin alone group. The difference is of unknown significance. The elevations were mostly asymptomatic. Ezetimibe does not alter lipid soluble vitamin status. It has no effect on the activity of the cytochrome P450 isoenzymes and no drug interactions have been observed with warfarin and oral contraceptives. However, cyclosporine may increase ezetimibe levels; thus, patients who take both ezetimibe and cyclosporine should be carefully monitored. As well, cholestyramine can decrease the bioavailability of ezetimibe. Thus, ezetimibe should be dosed at least 2 h before or 4 h after cholestyramine."

This article concludes with the statement that "ezetimibe is a safe, well tolerated and
effective addition to the current selection of LDL-lowering agents and will be particularly useful in those patients who either cannot achieve target LDL-C levels on an adequate dose of statin, or cannot tolerate or have contraindications to statins."

The CCOHTA newsletter’s section on Adverse Effects notes that "Ezetimibe alone or added to a statin did not significantly alter serious adverse event rates or withdrawal rates due to adverse events in eight- and 12-week trials. Liver function tests and monitoring are recommended when ezetimibe is combined with a statin, as an increase in the enzyme markers of liver damage was observed. Recent cases of angioedema and rash have been reported."

The newsletter’s summary includes one point on this issue: "The safety and tolerability of ezetimibe alone or combined with a statin has not been established in trials beyond 12 weeks."

These two safety and tolerability profiles are so radically different as to raise serious questions about the scientific objectivity and independence of the CJCP article.

James G. Heller, PhD, DECH
President, James G. Heller Consulting Inc.
Associate Professor, Public Health Sciences,
University of Toronto