

# The Medical Letter®

## On Drugs and Therapeutics

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### IN BRIEF

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#### Clopidogrel and Omeprazole

Use of a proton pump inhibitor (PPI) to protect against gastrointestinal (GI) bleeding in patients taking the antiplatelet agent clopidogrel (*Plavix*) may interfere with the activation of clopidogrel and diminish its antiplatelet effect, increasing the risk of cardiovascular events.<sup>1</sup> A randomized, placebo-controlled trial (COGENT) has found that use of the PPI omeprazole in patients taking clopidogrel in addition to aspirin decreased the incidence of GI bleeding without increasing the risk of a cardiovascular event, but the number of cardiovascular events was small and the formulation of omeprazole was atypical.<sup>2</sup> The FDA in the same issue of the same journal cautioned against concluding from the results of COGENT that concurrent use of clopidogrel and omeprazole is safe.<sup>3</sup>

To some extent, all PPIs reduce the enzymatic activity of CYP2C19, which is thought to be mainly responsible for the bioactivation of clopidogrel. Omeprazole is a strong inhibitor of CYP2C19; pantoprazole (*Protonix*, and others) appears to have less effect on CYP2C19 and not to attenuate the antiplatelet effect of clopidogrel.<sup>4-6</sup> Medical Letter consultants believe that patients at risk for upper GI bleeding who take clopidogrel should also take a PPI, but not omeprazole. Until more data become available on other PPIs, pantoprazole would be a reasonable choice.

1. PPI interactions with clopidogrel revisited. *Med Lett Drugs Ther* 2009; 51:13.
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3. MR Southworth and R Temple. Interaction of clopidogrel and omeprazole. *N Engl J Med* 2010; 363:1977.
4. DJ Angiolillo et al. Differential effects of omeprazole and pantoprazole on the pharmacodynamics and pharmacokinetics of clopidogrel in healthy subjects: randomized, placebo-controlled, crossover comparison studies. *Clin Pharmacol Ther* 2010; Sept 15 epub.
5. T Cuisset et al. Comparison of omeprazole and pantoprazole influence on a high 150-mg clopidogrel maintenance dose: the PACA (Proton Pump Inhibitors And Clopidogrel Association) prospective randomized study. *J Am Coll Cardiol* 2009; 54:1149.
6. H Neubauer et al. Pantoprazole does not influence the antiplatelet effect of clopidogrel – a whole blood aggregometry study after coronary stenting. *J Cardiovasc Pharmacol* 2010; 56:91.

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