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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.¹ 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.² 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.³

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.⁴⁻⁶ 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.
