Clinical Practice Assessment

**Clopidogrel (Plavix) in combination with omeprazole (Prilosec)**

**Clinical Question:** Does the combination of omeprazole (Prilosec) and clopidogrel (Plavix) result in increased cardiovascular events compared with clopidogrel alone?

**Bottom Line:** Some observational studies suggest an increase in cardiovascular events in patients on the combination (1, 2, 3) but others do not (4, 5). The only randomized, placebo-controlled trial (6) did not demonstrate reduced clopidogrel efficacy. The decision to prescribe this combination should be made following a thoughtful discussion between prescriber and patient weighing the risks, benefits and alternatives. This discussion should be well-documented in the chart.

**Synopsis:** Based on *in vitro* data, the FDA recently published a warning against using clopidogrel (Plavix) and omeprazole (Prilosec) in combination due to the potential for reduced clopidogrel effectiveness. While some observational studies suggest an increase in cardiovascular events in patients on the combination (1, 2, 3), others do not (4, 5). It remains unclear whether any potential effect is a class effect or PPI specific. A randomized, placebo-controlled trial (COGENT) compared dual antiplatelet therapy with and without omeprazole and found reduced upper GI bleeding without increased cardiovascular adverse outcomes in the omeprazole cohort (6). The risk of major bleeding for patients on dual antiplatelet therapy (aspirin and clopidogrel) with one additional risk factor for bleeding is reduced from 11.1% to 1.8% by the addition of a PPI (7). Significant risk factors include:

- History of upper GI bleed
- Peptic ulcer disease
- End stage renal disease
- Patients > 70 years of age

The Divisions of Cardiology and Gastroenterology believe the decision to prescribe this combination should be made following a thoughtful discussion between prescriber and patient weighing the risks, benefits and alternatives. Dean General Counsel recommends this discussion be well-documented in the chart. An actual consent form need not be signed. The American College of Gastroenterologist, American College of Cardiology Foundation, and the American Heart Association have recently published similar recommendations (8).
Sources:
2) Ho PM, et al. JAMA 2009;301(9):937-44.

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