

CLOPIDOGREL (PLAVIX)/PROTON PUMP INHIBITOR TREATMENT RECOMMENDATIONS IN CV PATIENTS

May 20, 2009

Dear Colleagues:

There has been recent clinically important evidence of adverse outcomes for patients who combine clopidogrel (Plavix) with proton pump inhibitors (PPI) post coronary artery stenting. This has led the Society of Cardiac Catheterization and Intervention (SCAI) and the FDA to issue warnings on this interaction. We are writing to communicate the Minneapolis Heart Institute[®]'s recommendations on this matter.

The Clopidogrel Medco outcomes found that patients who took clopidogrel for a full year following coronary stenting who concomitantly took a PPI had a 70percent increased risk in the combined event rate of heart attack and unstable angina and a 48percent increased risk of stroke. They similarly had a 35percent increase in the need for repeat coronary procedure. The event rates for the PPIs were as follows: Prevacid 24percent, Nexium 24 percent, Prilosec 25percent and Protonix 29percent, all statistically significant to no PPI control group at 17.9percent. The newer proton pump inhibitors rabeprazole (Aciphex) or dexlansoprazole (Kapidex) were not studied.

Clopidogrel is activated by the CYP enzyme system into a metabolite that has antiplatelet effects. The PPIs as a class have a negative effect on the CYP enzyme system thus blocking the conversion of clopidogrel to its active form. Population based studies do not show any negative effect of combined H2 blockers and clopidogrel.

For patients who have received a stent or who are post MI without a stent, PPIs have often been prescribed for a short duration to prevent the GI effects of dual antiplatelet therapy. However, many patients can be satisfactorily treated with H2 inhibitors

The Minneapolis Heart Institute[®] is urging health care providers in Minnesota to consider prescribing H2 blockers (such as ranitidine) instead of PPIs for patients taking clopidogrel.

The Minneapolis Heart Institute[®] has taken the following steps to address this important health care and patient safety issue:

1. Distribution of this letter and handout regionally.
2. Letters of information to our patients who have received stents within the past year.
3. Updated the Minneapolis Heart Institute[®] and Minneapolis Heart Institute Foundation (MHIF) websites to provide access to handouts and links to the important studies mentioned above.

We have always valued the important collaboration between primary care providers and the Minneapolis Heart Institute[®]. We hope that together we can effectively address this issue to the betterment of our patients. The links below to SCAI are excellent resources.

Please also be assured that going forward, we will address the need for appropriate antiulcer medication prior to any decision on coronary artery stenting or initiation of clopidogrel post MI.

Please feel free to contact any of us with any questions or comments.

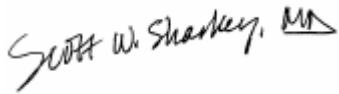
For better patient care,



Kevin J. Graham, MD
Director, Preventive Cardiology
President, Minneapolis Heart Institute[®]
At Abbott Northwestern Hospital
kgraham@mplsheart.com



Michael M. Mooney, M.D.
Director, Interventional Cardiology
Minneapolis Heart Institute[®] at Abbott
Northwestern Hospital
mmooney@mplsheart.com



Scott Sharkey, MD
Director, Cardiac Emergency Program
Minneapolis Heart Institute[®] at Abbott Northwestern Hospital
ssharkey@mplsheart.com

Referenced Web Links:

1. http://www.scai.org/drlt1.aspx?PAGE_ID=5870
2. http://www.fda.gov/cder/drug/early_comm/clopidogrel_bisulfate.htm
3. http://scai.org/pdf/Stanek_Clopidogrel-PPI_SCAI_2009.pdf

MEDICATION ALERT

Clopidogrel and Proton Pump Inhibitor (PPI) Drug-Drug Interaction

- Clopidogrel (Plavix®) is a blood thinner which is used to prevent blood clots that could lead to heart attacks or strokes in patients at risk for those problems.
- Recently published reports strongly suggest that the beneficial effect of clopidogrel is reduced, and the rate of adverse heart related events is increased when patients are also taking one of several medications called proton pump inhibitors (PPIs).
- PPIs are used to treat acid related stomach and throat problems such as stomach ulcers and acid reflux. Currently available PPIs include:

Generic Name	Trade Name	Available Source
Omeprazole	Prilosec®	Over-the-Counter AND by Prescription
Omeprazole/Sodium Bicarbonate	Zegerid®	Prescription Only
Esomeprazole	Nexium®	Prescription Only
Lansoprazole	Prevacid®	Prescription Only
Pantoprazole	Protonix®	Prescription Only
Rabeprazole	Aciphex®	Prescription Only

- Patients who are taking clopidogrel should continue to take clopidogrel.
- **Clopidogrel patients who are currently taking or considering taking a PPI should contact their health care provider to discuss alternatives.**
- Alternative acid reducing medications that do not cause this drug interaction include the histamine blockers famotidine, ranitidine, and cimetidine, as well as other traditional antacids such as Tums, Maalox, Mylanta, Amphojel, Pepto-Bismol and others.
- These studies were predominantly on patients that were within one year of having coronary artery stents placed. Many patients have been on clopidogrel and a PPI for longer than one year or for other reasons. There is no good data on longterm use of these two classes of drugs together. As with all medication decisions, individualization of treatment with your physician is important for the best outcome.