

WY-DUR

Wyoming Drug Utilization Review Board

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Dear Prescriber,

Recently, the American College of Cardiology Foundation, American Heart Association and the American College of Gastroenterology released a consensus statement on reducing gastrointestinal risks of antiplatelet therapy and use of non-steroidal anti-inflammatories¹. The following recommendations were made:

- Because the use of NSAIDs with cardiac-dose aspirin substantially increases the risk of ulcer complications, gastroprotective therapy should be prescribed for patients at-risk.
- The use of low-dose aspirin alone for cardiac prophylaxis increases the risk of upper gastrointestinal events by two- to four-fold. The risk increases with aspirin dose. For chronic therapy, doses above 81 mg should not be routinely prescribed.
- The combination of aspirin and anticoagulation therapy (heparin, LMWH, warfarin) increases the risk of major extracranial bleeding events, a large number of which occur in the upper GI tract. Patients requiring this combination should receive gastroprotective therapy. An INR of 2.0 – 2.5 is recommended when warfarin is added to aspirin plus clopidogrel.
- Substitution of clopidogrel for aspirin is not recommended for reducing the risk of recurrent ulcer bleeding. For prophylaxis of GI complications, it is inferior to the combination of aspirin plus a proton pump inhibitor.
- Combining clopidogrel with warfarin is associated with increased incidence of major bleeding compared with monotherapy.
- Proton pump inhibitors are the preferred agents for treating and preventing NSAID and aspirin associated gastrointestinal injury.

A treatment algorithm is included in the guidelines with the following recommendations:

- Patients with GI bleeding, dual antiplatelet therapy, concomitant anticoagulant therapy or a history of ulcer complications or disease should receive a proton pump inhibitor.
- Patients with none of the above, but with more than one risk factor (age >60, corticosteroid use, dyspepsia or GERD symptoms) should receive a proton pump inhibitor.
- Patients with a history of ulcer complications or disease should be tested for H. pylori and treated accordingly if positive.

The Food and Drug Administration has recently released an early communication regarding the potential effects of proton pump inhibitors on the effectiveness of clopidogrel². A seven-day study published in the Journal of the American College of Cardiology showed that omeprazole decreased the platelet inhibitory effect of clopidogrel³. However, the clinical significance of this effect is unknown. The manufacturers have agreed to conduct additional studies to determine the possible causes of interpersonal differences in clopidogrel effectiveness².

Some proton pump inhibitors may inhibit the cytochrome enzymes (CYP2C19) which convert clopidogrel to an active form⁴. This possible interaction is more likely with omeprazole and esomeprazole than the other proton pump inhibitors. There is no evidence to date showing that outcomes are better using one proton pump inhibitor over another.

In addition to Prilosec OTC, pantoprazole is currently on the Wyoming Medicaid Preferred Drug List and lansoprazole (Prevacid) will be added around April 1, 2009. This letter is intended to be educational only. All references are available upon request. Thank you for continuing to care for Wyoming Medicaid patients.

Sincerely,



Aimee Lewis, Pharm.D.
DUR Manager

References:

1. Bhatt D, Scheiman J, Abraham N, et al. ACCF/ACG/AHA 2008 Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use. *Circulation*. 2008;118:1894-1909.
2. Early Communication and Ongoing Safety Review: Clopidogrel bisulfate (marketed as Plavix) 1/26/2009. Available online at: <http://www.fda.gov/medwatch/safety/2009/safety09.htm#plavix>.
3. Gilard M, Arnaud B, Cornily J-C, et al. Influence of Omeprazole on the Antiplatelet Action of Clopidogrel Associated with Aspirin. *J Am Coll Cardiol*. 2008;51:256-260.
4. Reducing the risk for GI bleeding with antiplatelet drugs. *Pharmacist's Letter/Prescriber's Letter* 2008;24(12):241205.

*Affiliated with the University of Wyoming School of Pharmacy
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