UKM MEDICAL CENTRE

Pharmacy Bulletin

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Updates on Clopidogrel-Proton Pump Inhibitor

Early 2010, the US Food & Drug Administration issued a warning about a possible clopidogrel-omeprazole interaction that might diminish clopidogrel's platelet inhibition. Clopidogrel is commonly co-prescribed with Proton Pump Inhibitors to reduce the increased risk of gastrointestinal complications caused by antiplatelet drugs. The alert states that when clopidogrel and omeprazole are taken together, the effectiveness of clopidogrel is reduced. The mechanism that involved in the interaction was that certain PPIs may make clopidogrel less effective by inhibiting the enzyme that converts clopidogrel to the active form of the drug. Patients at risk for heart attacks or strokes who use clopidogrel to prevent blood clots will not get the full effect of this medicine if they are also taking PPIs.

However, recently one expert consensus meeting was held to discuss this safety issue. The ACCF*/ACG*/ AHA* 2010 Expert Consensus Document on the Concomitant Use of Proton Pump Inhibitors and Thienopyridines : A Focused Update of the ACCF/ACG/AHA 2008 Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy & NSAID Use objective was to review critically the recent development in this area, as many recent investigations of this potential adverse drug interaction have been performed.

- Clopidogrel reduces major CV events compared with placebo or aspirin
- Dual antiplatelet therapy with clopidogrel and aspirin, compared with aspirin alone, reduces major CV events in patients with established Ischemic heart disease, and it reduces coronary stent thrombosis but is not routinely recommended for patients with prior ischemic stroke because the risk of bleeding.
- Clopidogrel alone, aspirin alone, and their combination are all associated with increased risk of GI bleeding.
- Patients with prior GI bleeding are at highest risk for recurrent bleeding on antiplatelet therapy. Other clinical characteristics that increase the risk of GI bleeding include advanced age, concurrent use of anticoagulants, steroids or Nonsteroidal anti-inflammatory drugs (NSAIDS) including aspirin, and *Helicobacter pylori* infection. The risk of GI bleeding increases as the number of risk factors increases.
- Use of a PPI or histamine H2 receptor antagonist (H2RA) reduces the risk of upper GI bleeding compared with no therapy. PPIs reduce upper GI bleeding to a greater degree than do H2RAs.
- **PPIs are recommended to reduce GI bleeding among patients with a history of upper GI bleeding. PPIs are appropriate in patients with multiple risk factors for GI bleeding who require antiplatelet therapy.**
- **Routine use of either PPIs or H2RA is not recommended for patients at lower risk of upper GI bleeding, who have much less potential to benefit from prophylactic therapy.**
- **Clinical discussions regarding concomitant use of PPIs and thienopyridines must balance overall risks and benefits, considering both CV & GI complications.**
- Pharmacokinetic & pharmacodynamic studies, using platelet assays as surrogate endpoints, suggest that concomitant use of clopidogrel and a PPI reduces the antiplatelet effects of clopidogrel. The strongest evidence for an interaction is between omeprazole & clopidogrel. It is not established that changes in these surrogate endpoints translate into clinically meaningful differences.
- Observational studies and a single randomized clinical trial (RCT) have shown inconsistent effects on CV outcomes of concomitant use of thienopyridines and PPIs. A clinically important interaction cannot be excluded, particularly in certain subgroups, such as poor metabolizers of clopidogrel.
- The role of either pharmacogenomic testing or platelet function testing in managing therapy with thienopyridines and PPIs has not yet been established.

ACCF : American College of Cardiology Foundation
ACG : American College of Cardiology
AHA : American Heart Association

Announcement from Pharmacy Department

POTENTIAL MEDICATION ERROR ALERT!!

10mg/mL , 20mL (200mg/20mL) &
50*mg/mL, 10mL* (500mg/10mL).

Injection Ketamine is available in 2 strengths :

FOR YOUR DRUG INFORMATION :

- Always be informed and alert of the different strengths available
- Never order IV therapy by mL as they exist in different strengths. Order in mg.
- Please read/check the labels on the vial/ampoule multiple times.

Oseltamivir Suspension

Please note that starting January 2011, Royce Pharma will not be manufacturing the Oseltamivir Suspension 12mg/ml anymore. Hence, all syrup suspension will be prepared extemporaneously by Manufacturing Unit, Inpatient Pharmacy (ext 5811). Please note that the **STRENGTH** of the commercially available and extemporaneously prepared are **DIFFERENT.** Commercially available suspension by Royce Pharma is **12mg/mL**, while the suspension prepared extemporaneously by Manufacturing Unit is **15mg/mL.** The dosing for oseltamivir is as below :

	OLD PREPARATION 12mg/mL bY Royce Pharma		**NEW** (EXTEMPORANEOUS PREPARATION, 15mg/mL)	
	Treatment dose	**Prophylaxis dose**	**Treatment dose**	**Prophylaxis dose**
15kg or less	2.5 ml bd x 5 days	2 ml od x 10 days	2ml bd x 5 days	2 ml od x 10 days
16kg to 23kg	3.75 ml bd x 5 days	3 ml od x 10 days	3 ml bd x 5 days	3 ml od x 10 days
24kg to 40kg	5 ml bd x 5 days	4 ml od x 10 days	4ml bd x 5 days	4 ml od x 10 days
40 kg or more	6.25 ml bd x 5 days	5 ml od x 10 days	5 ml bd x 5 days	5 ml od x 10 days

Storage : Stable for 35 days (fridge) from 2-8 °C or 5days at room temperature (25 °C)

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Gong Xi Fa Chai!

We would like to wish our counterparts a joyous and prosperous New Year. May you have nothing but good fortune this Year of the Rabbit.