Drug Safety Advice Clopidogrel + PPIs
– Action in NHS Borders Reviewed April 2010.

Summary:

- **All NHS Borders patients prescribed clopidogrel +omeprazole or esomeprazole require review of this combination at their next consultation. For the majority of patients, omeprazole or esomeprazole can be safely switched to lansoprazole.**
- **Patients newly commenced on clopidogrel requiring PPI should be prescribed lansoprazole.**
- Patients on clopidogrel + cimetidine should be reviewed.
- Consultants advice is available for "problematic" patients.
- Decisions should be appropriately documented.
- Additionally, patients taking clopidogrel should not be commenced on fluoxetine, fluvoxamine, cimetidine, moclobemide, ticlopidine, carbamazepine, oxcarbazepine, and chloramphenicol unless risks outweigh benefits.

Drug safety update Volume 3, Issue 9. April 2010 from MHRA offers the following advice:

- **Concomitant use of clopidogrel and omeprazole or esomeprazole is to be discouraged unless considered essential**
- **Doctors should check whether patients who are taking clopidogrel are also buying OTC omeprazole and consider whether other gastrointestinal therapies would be more suitable**
- **Pharmacists should check whether patients buying omeprazole are also taking clopidogrel**
- **Consider PPIs other than omeprazole or esomeprazole in patients who are taking clopidogrel. Other gastrointestinal therapy such as H_2 blockers (except cimetidine) or antacids may be more suitable in some patients.**
- **Discourage concomitant use of other known CYP2C19-inhibiting medicines with clopidogrel because these are expected to have a similar effect to omeprazole and esomeprazole (CYP2C19 inhibitors include fluvoxamine, fluoxetine, moclobemide, voriconazole, fluconazole, ticlopidine, ciprofloxacin, cimetidine, carbamazepine, oxcarbazepine and chloramphenicol)**

The cardiology, GI and stroke teams, primary care prescribing group and BGH pharmacy team support the following action:

- **All patients currently prescribed omeprazole or esomeprazole + clopidogrel should have this combination reviewed at their next appointment / hospital admission. The majority of patients who are prescribed omeprazole or esomeprazole (and require ongoing prescription of clopidogrel) can be safely switched to lansoprazole (If H_2 blocker indicated – prescribe ranitidine)**
- **If PPI indicated for new start clopidogrel patients, prescribe lansoprazole**
- **Different GI risks associated with different patient populations should be taken into consideration** – e.g patients who are prescribed clopidogrel long term for secondary prevention of stroke, and patients on one month's treatment with clopidogrel (+ aspirin) post STEMI.

The NHS Borders gastroenterology consultants (Drs Chris Evans, Jonathan Fletcher and Jonathan Manning) are available to advise on appropriate GI cover for patients where either GPs or consultants are unsure of the best option.
The NHS Borders cardiology consultants (Drs Paul Neary and Helen Oxenham) and stroke consultants (Drs Susan Kerr and Paul Syme) are also available to discuss and support decisions relating to prescribing of clopidogrel.

The above consultants may be contacted either by email or letter. The stroke consultants may also be contacted by mobile phone (07500917139)

Sanofi Aventis
http://emc.medicines.org.uk/document.aspx?documentId=9484 also suggest that there may be a similar interaction between clopidogrel and other drugs which, like the PPIs omeprazole and esomeprazole, inhibit CYP2C19.
NHS Borders cardiology, gastroenterology, neurology, stroke, psychiatry and microbiology teams issue this updated advice in October 2009 based on an assessment of current best evidence.

- Where an SSRI antidepressant is indicated for a patient who is currently prescribed **clopidogrel, fluoxetine** should not be commenced (**citalopram** is an appropriate alternative).
- If **fluvoxamine or moclobemide** are indicated for a patient prescribed **clopidogrel**, potential risks and benefits of the combination should be assessed.
- Patients taking the combination of **cimetidine + clopidogrel** - review and consider switch from cimetidine to ranitidine.
- **Voriconazole, fluconazole** and **ciprofloxacin** interact with **clopidogre**l, but as use of these antifungals/antibiotics is generally limited to short duration, there is currently no requirement to avoid this combination.
- **Carbamazepine** also interacts with **clopidogrel**. Patients who are prescribed **clopidogrel** should not be commenced on **carbamazepine**. Dr David Simpson, consultant neurologist, should be consulted for advice on choice of appropriate anti-epileptic. Where **clopidogrel** is initiated for patients with epilepsy, who are currently stable on **carbamazepine**, patients should continue with **carbamazepine.**
- Patients who are being switched from **high-dose PPIs** (daily doses above either 20mg omeprazole or lansoprazole 30mg) should have the dose titrated down, weekly, to avoid rebound hyper-acidity. Cover with **ranitidine** may be necessary during the titration period. (Note that patients with Barretts oesophagitis should remain on a PPI).

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