

CLOPIDOGREL & POSSIBLE INTERACTION BETWEEN PROTON PUMP INHIBITORS

This bulletin supersedes PostScript Extra No 16, October 2009

This bulletin has been revised to reflect the updated guidance from the European Medicines Agency, Mar 2010

- There is a possible interaction between clopidogrel and the proton pump inhibitors (PPIs), omeprazole and esomeprazole.
- Prescribers should avoid the use of omeprazole and esomeprazole with clopidogrel where possible.
- Prescribers should consider if concomitant therapy with clopidogrel and a PPI is appropriate. Is clopidogrel indicated? Has aspirin been tried previously? Is there a need for a PPI?
- If clopidogrel is indicated and the patient requires a PPI, the NHSGGC formulary choice would be lansoprazole.

Background

- In 2009, the European Medicines Agency (EMA) and the UK Medicines and Healthcare Products Regulatory Agency (MHRA) issued advice on the possible interaction between clopidogrel and proton pump inhibitors (PPIs).^{1,2} They advised that concomitant use of a PPI with clopidogrel should be avoided unless considered essential.
- Following this, the NHS Greater Glasgow & Clyde Heart Disease Managed Clinical Network (MCN) issued a consensus statement. The full statement was published in PostScript No 52, July 09 and is available on the GGC Formulary website <http://www.ggcformulary.scot.nhs.uk>.³
- Subsequently, PostScript Extra No. 16, Oct 2009 was published which discussed common clinical scenarios for patients who were prescribed clopidogrel and a PPI.⁴
- Since then there has been updated advice issued by the EMA.⁵ This bulletin supersedes PostScript Extra No. 16 to reflect this latest advice.

Latest Advice

In March 2010, the EMA published an update to the interaction warning between clopidogrel and PPIs.⁵ Following an analysis of new data, the existing warning over the concomitant use of clopidogrel-containing medicines has been amended. The class warning for all PPIs has been replaced with a warning stating that **only the concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged**.

The current evidence does not support extending this

advice to other PPIs. However, because it is not possible to completely exclude a possible interaction with these PPIs on the basis of available data, the potential risk of a slight reduction in efficacy of clopidogrel should be weighed against the potential gastrointestinal (GI) benefit of the PPI.⁶

Prescribing Notes

For patients currently on clopidogrel & a PPI or if you plan to prescribe clopidogrel with a PPI, the following points should be considered:

- For patients prescribed clopidogrel antiplatelet monotherapy, reassess the need for clopidogrel versus aspirin. Follow the NHSGGC antiplatelet guideline and consider changing to aspirin unless aspirin contra-indicated or aspirin and a PPI previously not tolerated.⁷
- Is gastroprotection indicated? Patients should only be prescribed gastroprotection if there is a clear clinical need or if patients are at high risk of a GI bleed.
- Some of the high risk factors for a GI bleed include a history of GI bleeding, history of peptic ulcer disease, concomitant therapy with both NSAIDs and aspirin, oral corticosteroids, anticoagulants, selective serotonin re-uptake inhibitors (SSRIs), alcohol intake and advancing age.
- If gastroprotection is indicated and the patient remains on clopidogrel, lansoprazole would be the NHSGGC formulary choice of PPI.⁸ Alternatively, ranitidine may be considered.

REFERENCES

1. European Medicines Agency (EMA). Public statement on possible interaction between clopidogrel and proton pump inhibitors, 29/05/09. Accessed via <http://www.ema.europa.eu>.
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3. NHS Greater Glasgow & Clyde. Postscript No 52, July 2009. Accessed via <http://www.ggcformulary.scot.nhs.uk>.
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5. European Medicines Agency (EMA). Public statement on interaction between clopidogrel and proton-pump inhibitors, 17/03/2010. Accessed via <http://www.ema.europa.eu>.
6. Medicines and Healthcare Products Regulatory Agency (MHRA). Clopidogrel and proton pump inhibitors: interaction-updated advice. Drug safety update, Vol 3, Issue 9, Apr 2010. Accessed via <http://www.mhra.gov.uk>.
7. NHSGGC Antiplatelet guideline 2008. Accessed via <http://www.ggcformulary.scot.nhs.uk>
8. NHSGGC, The Greater Glasgow & Clyde Formulary, 3rd Ed, Aug 2009.