UPDATED NHSGGC ANTI-PLATELET GUIDELINES

PostScRxipt
from the
NHSGGC Area Drug & Therapeutics Committee
Issue 45 May 2008

The updated NHSGGC anti-platelet guidelines, which were developed by the Heart MCN, have now been approved by the ADTC. They can be accessed in full on the guidelines area of our website.

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Website
http://www.ggcformulary.scot.nhs.uk

Primary prevention
Aspirin dispersible 75mg daily is indicated for use in high-risk individuals with a 10-year cardiovascular risk ≥ 20%. These are:
- patients with diabetes aged > 50 years
- patients with diabetes aged < 50 years with hypertension or target organ damage
- patients with familial hypercholesterolaemia.

GPs are encouraged to review other groups of adults where this level of risk is likely to determine if they should be offered primary prevention. These include individuals over 40 years of age who fall into the following categories:
- smokers
- patients with hypertension
- patients with hypercholesterolaemia
- patients with family history of premature coronary heart disease or stroke (males < 45 years; females < 55 years) in first degree relatives (parents or siblings).

There are no reported studies to support the use of clopidogrel or dipyridamole in primary prevention.

Secondary prevention
Life-long treatment with dispersible aspirin 75mg daily should be offered to all patients with a diagnosis of:
- CHD (angina, acute coronary syndrome, post-CABG)
- thrombotic stroke or TIA
- peripheral arterial disease (intermittent claudication or post-graft).

Ideally, BP should be controlled (<150/90mmHg) before starting any anti-platelet agent. New NHSGGC guidelines on the treatment of hypertension will be published shortly. Unless contraindicated, dispersible aspirin 75mg per day, once commenced, should be administered for life, unless an indication for warfarin develops.

Contraindications to aspirin are rare but include aspirin allergy (aspirin induced angioedema, asthma or skin rash). Contraindications for all anti-platelet agents include:
- recent GI bleed (previous six months)
- proven active peptic ulcer disease
- haemophilia or other bleeding disorder.

Clopidogrel 75mg per day is only used for secondary prevention if aspirin is contraindicated or the side effects are intolerable despite modification of contributory factors and treatment with a formulary PPI.

Combination anti-platelet regimens
Combination therapy with aspirin increases the risk of adverse effects and should only be used for the following scenarios:

Indication	Group	Additional treatment (aspirin 75mg daily indefinitely +)	Course length
Thrombotic stroke or TIA	All patients	Dipyridamole MR 200mg twice daily	Indefinite
Carotid artery stent	All patients	Clopidogrel 75mg daily	4 weeks
Acute coronary syndromes (no PCI or stent)	ST elevation MI	Clopidogrel 75mg daily	4 weeks
	Non-ST elevation MI	Clopidogrel 75mg daily	12 weeks
Coronary artery stent	Bare metal stent (elective)	Clopidogrel 75mg daily	4 weeks
	Bare metal stent (unstable)	Clopidogrel 75mg daily	12 weeks
	Drug eluting stent	Clopidogrel 75mg daily	52 weeks

For those patients who suffer recurrent ischaemic stroke on aspirin + dipyridamole, there is insufficient evidence to support the use of clopidogrel in place of, or in addition to, aspirin. Such patients should be referred for individualised specialist advice from a stroke service.

The combination of warfarin and an anti-platelet agent is associated with a significantly higher major haemorrhage complication rate than either agent alone, without offering any proven benefit in reducing ischaemic or thrombo-embolic events (except in patients with metallic prosthetic heart valves). The full guideline has details on how to manage patients on one who develop an indication for the other.

GI symptoms and use of aspirin
In patients with a history of bleeding peptic ulcer disease, the combination of aspirin + PPI is safer than clopidogrel

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For all article references, check our website
http://www.ggcformulary.scot.nhs.uk

Alphabetical list of most recent ADTC decisions

For full details of SMC advice, visit **www.scottishmedicines.org** For NICE advice, visit **www.nice.org.uk** For previous ADTC decisions, visit **www.ggcformulary.scot.nhs.uk**

Drug	Indication under consideration (There may be other licensed indications)	NHSGGC decision	
Bevacizumab (Avastin®)	First-line treatment of advanced and/or metastatic renal cell cancer in combination with interferon alfa-2a.	Non-*Formulary*.	x
Daptomycin (Cubicin®)	Treatment of Staphylococcus aureus bacteraemia when associated with right-sided infective endocarditis or with complicated skin and soft-tissue infections in adults.	*Formulary*. (Total *Formulary*.) Acknowledge new indication. Restricted to use on the advice of a microbiologist or infectious diseases physician for VRE, VISA, VRSA2 or patients not responsive to, or intolerant to, glycopeptide.	✓R
Diclofenac injection (Dyloject®)	Treatment or prevention of post-operative pain by intravenous injection in supervised healthcare setting.	Non-*Formulary*. Insufficient benefit over existing presentations and risk management issues of having multiple presentations available for different administration routes.	x
Efavirenz 600mg, emtricitabine 200mg, tenofovir 245mg (Atripla®)	HIV-1 infection in adults with virologic suppression to HIV-1 RNA levels of < 50 copies/ml on their current combination therapy for more than three months. Patients must not have experienced virological failure on any prior antiretroviral therapy and must be known not to have harboured virus strains with mutations conferring significant resistance to any of the three components contained in this fixed dose combination prior to initiation of their first antiretroviral treatment regimen.	*Formulary*. (Total *Formulary*.) Acknowledge new formulation. Restricted to use by HIV specialists.	✓R
Etoricoxib (Arcoxia®) (ADTC Appeal)	Symptomatic relief of osteoarthritis for patients in whom a COX-2 inhibitor is appropriate but who have documented sensitivity to sulphonamide agents.	Non-*Formulary*.	x
Follitropin alfa/lutropin alfa (Pergoveris®)	Stimulation of follicular development in women with severe LH and FSH deficiency.	Non-*Formulary*.	x
Infliximab (Remicade®)	Severe, active Crohn's disease in paediatric patients aged 6-17 years who have not responded to conventional therapy including a corticosteroid, an immunomodulator and primary nutrition therapy; or who are intolerant to, or have contraindications for, such therapies.	*Formulary*. (Total *Formulary*.) Acknowledge new indication. Restricted to specialist use.	✓R
Insulin glargine pre-filled pen (Lantus SoloStar®)	Diabetes mellitus in adults, adolescents and children of 6 years or above where insulin is required.	*Formulary*. (Preferred List.) Acknowledge new formulation. Restricted to initiation by consultant diabetologists in patients with severe/frequent nocturnal hypoglycaemia. Not for routine use in type 2 diabetes unless patients suffer from recurrent hypoglycaemia or require assistance with their insulin injections.	✓R
Insulin glulisine pre-filled pen (Apidra SoloStar®)	Treatment of adult patients with diabetes mellitus in whom treatment with this insulin analogue is appropriate and in whom the use of a pre-filled pen offers advantages over a pen and cartridge device.	*Formulary*. (Total *Formulary*.) Acknowledge new formulation. Restricted to use in patients where regular human insulin is appropriate.	✓R
Losartan/ hydrochlorothiazide (Cozaar Comp 100/12.5®)	Hypertension in patients whose blood pressure is not adequately controlled on hydrochlorothiazide or losartan monotherapy.	Non-*Formulary*.	x
Maraviroc (Celsentri®)	In combination with other antiretroviral medicinal products, for treatment-experienced adult patients infected with only CCR5-tropic HIV-1 detectable.	Non-*Formulary*.	x
Mesalazine (Mezavant XL®)	Induction of clinical and endoscopic remission in patients with mild to moderate active ulcerative colitis, and for maintenance of remission.	*Formulary*. (Preferred List.) Acknowledge new formulation.	✓
Methadone (Eptadone®)	Opiate dependence	Non-*Formulary*. This is a colourless, lemon-flavoured solution available in two strengths. In consultation with the Addiction Services, it was agreed not to add this product to the *Formulary* due to the potential risks of two indistinguishable strengths and a potentially more palatable formulation leading to increased dangers with unintentional ingestion.	x
Methoxy polyethylene glycol-epoetin beta (Mircera®)	Anaemia associated with chronic kidney disease.	*Formulary*. (Total *Formulary*.) Restricted to specialist initiation. Darbepoetin remains the preferred choice.	✓R
Nelarabine (Atriance®)	T-cell acute lymphoblastic leukaemia and T-cell lymphoblastic lymphoma whose disease has not responded to, or has relapsed following, treatment with at least two chemotherapy regimens.	Non-*Formulary* at this time. Deferred to allow consultation with the Regional Cancer Advisory Group.	?
Paliperidone (Invega®)	Schizophrenia.	Non-*Formulary*.	x
Retapamulin (Altargo®)	Short term treatment of the following superficial skin infections: impetigo and infected small lacerations, abrasions or sutured wounds.	Non-*Formulary*.	x
Salmeterol / fluticasone (Seretide 500 Accuhaler®)	Symptomatic treatment of patients with COPD with an FEV-1 from 50% to <60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations who have significant symptoms despite regular bronchodilator therapy.	Non-*Formulary* for this indication.	x
Valsartan 320mg (Diovan®)	Hypertension.	*Formulary*. (Total *Formulary*.) Acknowledge new formulation. Restricted to second line use in patients with a significant cough on an ACE inhibitor.	✓R
Vildagliptin (Galvus®)	Type 2 diabetes mellitus as dual oral therapy in combination with metformin.	*Formulary*. (Total *Formulary*.) Restricted to initiation on the advice of a specialist, in combination with metformin, only when the addition of a sulphonylurea is not appropriate, for patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin. In primary care, it is expected that initiation would follow interaction between the GP/ Diabetic Specialist Nurse and the consultant contact within the acute sector.	✓R
Zoledronic acid infusion (Aclasta®)	Treatment of osteoporosis in post-menopausal women at increased risk of fractures.	Non-*Formulary* at this time. Deferred to allow consultation with the Osteoporosis Group.	?

✓= *Formulary* ✓R = *Formulary* (restricted) **x** = non-*Formulary* **?** = awaiting final decision

Changes to *Formulary* status of rosiglitazone

The European Medicines Agency (EMEA) released a press statement in January 2008 recommending that a new warning be included in the Summary of Product Characteristics stating that the use of rosiglitazone in patients with ischaemic heart disease and/or peripheral arterial disease is not recommended. The EMEA also recommended a new contraindication be included that rosiglitazone must not be used in patients with acute coronary syndrome (ACS), such as angina or myocardial infarction, because the medicine has not been studied in controlled trials in this patient group.

ADTC statement on the *Formulary* status of rosiglitazone

In light of the EMEA advice and after consultation with the Diabetes Managed Clinical Network, the following changes to the NHSGGC *Formulary* status of rosiglitazone and the rosiglitazone/ metformin combination products have been agreed:

- Rosiglitazone has been removed from the Preferred List section of the *Formulary*.
- Rosiglitazone and rosiglitazone/metformin preparations remain in the Total *Formulary* section of the *Formulary*.
- In addition to existing restrictions, rosiglitazone and rosiglitazone/metformin preparations are restricted to initiation by, or on the advice of, a consultant diabetologist.

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NHSGGC policy on safe and secure handling of medicines for acute sites

For many years, all hospital sites in Greater Glasgow and Clyde have had policies relating to the safety and security of medicines. Many of these policies were based on the original Duthie Report from 1988. Since then, many changes in healthcare have occurred, including shorter in-patient stays, the introduction of non-medical prescribing and the routine systematic use of patients' own drugs, where possible, for in-patients. The Royal Pharmaceutical Society issued a revised Duthie Report in 2005. In addition, changes in the legislation around Controlled Drugs, prompted by the Shipman enquiry, have meant that a contemporary and harmonised policy on the safety and security of medicines was required for all acute sites.

The policy has been extensively reviewed by medical, nursing and pharmacy staff from all directorates and sites. It will be launched in a site-by-site manner, starting mid-May and continuing through June. At each site 'launch', short presentations will be held throughout the day to inform staff of the main points. Copies of the policy and supporting documentation will be distributed on that day to every ward, theatre and department on site.

The policy can be accessed via Staffnet using the following links:
In Glasgow - **www.staffnet/Info+Centre/Policies/Safe+and+Secure+Handling+of+Medicines/**
In Clyde - **www.staffnet.ggc.scot.nhs.uk/Info+Centre/Policies/Safe+and+Secure+Handling+of+Medicines/**

Any comments or queries on the policy can be made by e-mailing **sshm@ggc.scot.nhs.uk**

Webwatch:

***Drug and Therapeutics Bulletin* (DTB)**

The DTB is now available online at www.dtb.bmj.com/ with access through subscription or using an Athens password. Athens is an Access Management System which controls access to all resources held on subscription by NHS Scotland. NHS Scotland staff, students and partners can register for a password at www.elib.scot.nhs.uk

The DTB aims to provide informed and unbiased assessments of drugs and other treatments focusing on efficacy, safety, convenience and cost in relation to other available treatments. It comments on how drugs or other treatments should be used and aims to assess their place in overall management, giving practical advice on the overall management of disease. DTB also comments on how treatments are marketed and promoted, on the quality of the information available to prescribers and patients, and on the indications for which the treatment has been licensed.

There is an online archive of all monthly issues back to 1994 when fluticasone, tramadol and gabapentin were newly launched drugs. More recently, DTB has considered new drugs Grazax®, lidocaine plasters and buprenorphine for opioid dependence as well as topics such as:
- Do omega-3 fatty acids help in depression?
- Understanding monoclonal antibodies
- Topical negative pressure for chronic wounds
- Acupuncture for osteoarthritis of the knee.

NHSGGC anti-platelet guidelines *contd from page 1*

alone (for secondary prevention). For patients developing GI symptoms after starting aspirin, the following algorithm should be followed:

Consider and modify contributory factors, eg excess alcohol, NSAID use (OTC or prescribed).

If GI symptoms persist, despite modification of contributory factors

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ADD treatment dose PPI.
Enteric coated aspirin does NOT reduce GI symptoms – not recommended.

↓

Patient complying and GI symptoms persist? (rare)

↓

Change to clopidogrel 75 mg per day (secondary prevention only) **and stop PPI. Seek specialist gastroenterology advice if symptoms do not resolve.**

***Formulary* status of rosiglitazone** *contd from page 3*

Information for prescribers
- Patients with ischaemic heart disease, peripheral arterial disease or ACS who are currently receiving rosiglitazone should have their treatment reviewed by a diabetes clinic at the earliest opportunity. If the use of a thiazolidinedione is found to be beneficial in an individual patient, as demonstrated by a reduction or maintenance of a low HbA1c, the alternative *Formulary* thiazolidinedione, pioglitazone, should be initiated and re-titrated according to response.
- Patients currently receiving rosiglitazone who do not have ischaemic heart disease, peripheral arterial disease or ACS should have their treatment reviewed at their next scheduled diabetes clinic review.
- Diabetes specialists are willing to offer advice to clinicians on an individual patient basis where that is required.
- The Diabetes MCN is reviewing its guidance on the management of diabetes and further information will be available in due course.

NHS Greater Glasgow and Clyde

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