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Dual Antiplatelet Therapy

Clopidogrel or ticagrelor are indicated as part of a dual anti-platelet therapy (DAPT) regimen along with indefinite aspirin for management of patients with acute coronary syndrome (ACS) and / or undergoing percutaneous coronary intervention (PCI). The NHSGGC Guideline for Antiplatelet Therapy in Secondary Prevention of Coronary Heart Disease makes recommendations for DAPT duration in accordance with clinical circumstances.

Risks of inappropriate treatment

Concerns have been raised previously about the potential for patients to be continued on treatment after the anticipated stop date. Extended treatment means that patients continue to be exposed to the risk of adverse effects without additional clinical benefit.

Systems have been put in place to prevent inappropriate continuation of DAPT. These include the immediate discharge letter stating recommended duration of therapy, the patient and their GP being provided with an information leaflet and in the case of patients undergoing PCI at Golden Jubilee National Hospital (GJNH), a letter from the Prescribing Team advising the GP when DAPT should be stopped. Despite this, DAPT might not always be stopped at the correct time.

Auditing practice

Prescribing was audited in Glasgow North East during April and May 2014.

- 43 practices were involved
- 631 patients were reviewed; an average of 15 per practice.
- 81% of patients had DAPT commenced on a cardiology ward or directly by GJNH.

- General medical, medicine for the elderly and surgical wards were responsible for a small proportion of initiations.
- The intended duration of therapy was generally readily identifiable.

The [antiplatelet guideline](#) published in May 2013 recommended that patients receiving a drug-eluting stent should generally be prescribed DAPT for 26 weeks. The audit identified that:

- 26% of patients had therapy recommended for 26 weeks
- Approximately one third of patients were recommended 12 weeks' therapy
- Another third were recommended a duration of 52 weeks (in line with previous advice).
- 17 patients had 52 weeks therapy requested post-guideline launch (June 2013 onwards)
- 4 patients had lifelong DAPT specified.
- Reason for therapy duration deviating from the guideline was not always recorded.

70% of patients had emergency or elective PCI with the rest managed medically. Patients treated medically should receive 12 weeks of therapy; this correlates well with actual practice.

Almost 40% of patients (237) exceeded the intended duration; 77% of these were prescribed clopidogrel and 19% received ticagrelor.

- A total of 7,537 weeks of excess therapy was prescribed
- This averages 12 weeks per patient
 - range 1 – 504 weeks
- The cost of excess treatment was £8,386. The cost of clopidogrel has reduced dramatically in recent years; if this pattern to continued, but with ticagrelor as the predominant agent, costs would have been in excess of £100,000.

Almost half of the patients undergoing PCI at GJNH had Prescribing Team correspondence recommending DAPT cessation in the patient record. A notable difference existed in the average excess duration between the groups who did receive a letter (20 weeks) and did not receive a letter (41 weeks). Just over half the patients received the correct duration of treatment and that was irrespective of whether the practice received a letter.

Changing practice following audit

A variety of actions and evaluations were undertaken as a direct result of the audit:

- 157 clinical interventions were undertaken
- In 90 cases inappropriate DAPT was discontinued.
- This prevented an ongoing annual drug cost of £7,700.
- 26 patients had the intended stop date annotated on their prescription in accordance with best practice, as outlined in *PostScript Primary Care* (September 2013) http://www.ggcprescribing.org.uk/media/uploads/ps_primary_care/pspc_september_2013.pdf.

Practices are advised to review processes for managing advice on duration of DAPT therapy, eg by use of stop dates on the prescription.

Safety Update: Domperidone

The [MHRA](#) has recently recommended changes to the use of domperidone, including restricting the dose and duration of use, to minimise the known risks of potentially serious cardiac adverse effects.

There are now no drugs on the UK market licensed as prokinetic agents. Metoclopramide has also recently had restrictions placed on its use due to extrapyramidal adverse effects. It should only be used short-term (up to 5 days) and should not be used in chronic conditions such as gastroparesis, dyspepsia and GORD, nor as an adjunct in surgical and radiological procedures.

- Domperidone is now only licensed for nausea and vomiting.
- Domperidone should be used at the lowest effective dose for the shortest possible duration. The maximum treatment duration should not usually exceed one week.
- The new recommended dose in adults (and adolescents ≥ 35 kg where licensed) is 10mg orally up to three times daily (maximum dose of 30mg daily). Adults and adolescents weighing ≥ 35 kg may be given 30mg twice daily rectally as suppositories.
- In children under 12 years of age and less than 35kg, the recommended maximum oral dose is 0.25mg/kg body weight up to three times a day.
- Domperidone is contraindicated in severe hepatic impairment, conditions where cardiac conduction is, or could be, impaired or where there is underlying cardiac disease, and when co-administered with QT-prolonging medicines or potent CYP3A4 inhibitors.

Advice on alternative management of patients with GORD / dyspepsia and gastroparesis has been

produced by UKMI and is available at <http://www.midlandsmedicines.nhs.uk/filestore/domperidone%20GI%20restrictions%20May%202014.pdf>

Medicines for Children, a partnership of bodies including the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists' Group has information on use of domperidone in children at <http://www.medicinesforchildren.org.uk/search-for-a-leaflet/domperidone-for-gastro-oesophageal-reflux/>.

Practices have already been advised on appropriate timescales and mechanisms for managing this change.

PPIs and Clostridium Difficile

Clostridium difficile infection (CDI) is one of the important healthcare associated infection in Scottish hospitals. It is life-threatening (reported mortality rate 10 - 30%) and has the potential for person to person spread within healthcare settings. Particularly at risk are patients who are aged > 65 years, frail, immunocompromised or who have chronic obstructive pulmonary disease or cardiovascular disease. Across Scotland, rates of CDI have levelled off after a period of significant decreases but there is a need for new strategies to address the burden of CDI that still remains.

PPIs have been identified as a risk factor for CDI but, historically, the evidence has been conflicting. Four recently published meta-analyses provide further evidence that the use of PPIs can increase the risk of CDI and its recurrence, albeit there is general agreement with regards the low quality of available evidence. The recently published [CDI guidelines](#) from Health Protection Scotland, suggest that consideration should be given to stopping or reviewing the need for PPIs in patients with or at high risk of CDI.

There is also evidence that PPIs may be linked to other adverse clinical outcomes, while a number of studies (from the UK and the US) suggest that between 60-86% of PPIs may be being used inappropriately.

A significant amount of work has been undertaken in recent years in primary care to ensure PPI therapy is reviewed regularly. There is also guidance available on [prescribing PPIs for patients discharged from hospital](#).

This additional information reminds prescribers of the need for ongoing review of patients prescribed PPIs to consider whether doses can be decreased or therapy stopped rather than continued indefinitely.

Drug induced photosensitivity

At this time of year, with improving weather and the peak holiday period, the incidence of reactions to sun increase. Some medicines cause particular problems. Dr Paula E Beattie, Consultant Dermatologist at the Royal Hospital for Sick Children described some of the issues.

Drug photosensitivity reactions occur when a drug or metabolite within the skin interacts with ultraviolet (UV) radiation in sunlight. The drug may be ingested, injected or rarely applied topically. The vast majority of photosensitive reactions are phototoxic reactions.

The majority of drugs absorb UV wavelengths. A phototoxic reaction occurs when the drug present in the skin absorbs UV wavelengths specific to that chemical, becomes excited and produces a photochemical reaction which damages cellular components resulting in inflammation.

It can occur in any subject with sufficient exposure to the drug and to UV radiation; for example, doxycycline at a dose of 100mg will photosensitise 10-20% of individuals in Western Europe but at a dose of 200mg in summer months or in sunnier climates will photosensitise a much higher proportion.

- exposed site telangiectasia can occur when calcium channel antagonists target blood vessels
- increased skin fragility and blistering (pseudoporphyria) can occur with NSAID, tetracyclines, furosemide, amiodarone and fluroquinolones
- photo-onycholysis, where the nail separates from the bed, can occur with doxycycline.

A small proportion of reactions may be attributed to mechanisms other than phototoxicity, see below. Many will cause a typical pattern of reaction but some may cause photosensitivity by more than one mechanism, eg phenothiazines.

Photosensitivity types	Drugs implicated
Porphyria	Oestrogens Barbiturates Griseofulvin
Lupus erythematosus	Thiazides Hydralazine Tetracyclines
Photoallergy	Phenothiazines NSAIDs
Pellagra	Isoniazid

Photoallergy is a rare type IV hypersensitivity reaction which occurs most commonly with a topical chemical, eg sunscreen or NSAIDs, to form a photoallergen which presents as an exposed site dermatitis.

Knowledge of drug interaction with wavelength absorption can inform advice to patients on duration of photoprotection required. Potentially scheduling evening dosing of drugs such as fluroquinolones which have a short effect may help avoid phototoxicity.

Advice to patients when prescribing a potentially phototoxic drug

- Use photoprotection, including clothing and hats. Clothing should be of a fine weave so that light is not transmitted when held up to the light.
- Avoid the sun between the hours of 11am and 3pm and seek shade when outdoors. Note that shade from trees and umbrellas is not total shade and that variable exposure still occurs. UVA can also be transmitted through glass.
- Sunscreen should be very high factor. Most individuals apply it at a thickness that achieves a SPF 5-20 from an SPF50 sunscreen. Apply liberally and reapply frequently.
- Sunscreens can be prescribed in primary care only for protection in abnormal cutaneous photosensitivity resulting from genetic disorders or photodermatoses including vitiligo, those resulting from radiotherapy; chronic or recurrent herpes labialis. The NHS GGC Preferred List option is Sensense Ultra (SPF 50+).

Photosensitising Drugs	
Antibiotics	fluroquinolones, tetracyclines, sulphonamides
Antifungals	Griseofulvin
Diuretics	Thiazides, Furosemide
Cardioactive	Amiodarone, Quinidine
NSAIDs	Naproxen, Piroxicam
Ca channel blocker	Nifedipine, Benoxaprofen
Psychoactive agents	Phenothiazines, Chlorpromazine
Dermatology drugs	Psoralens, Retinoids
PDT agents	Foscan, Photofrin

Various patterns of phototoxicity are recognised:

- most manifest as an exaggerated sunburn reaction and so the diagnosis is often missed
- recurrent immediate erythema (redness) can give way to a chronic exposed site dermatitis with drugs given long term, eg thiazides.
- recurrent phototoxicity may sometimes be associated with photocarcinogenesis, eg voriconazole.
- an immediate prickling, burning, erythema and swelling can also be seen, sometimes with delayed erythema and pigmentation. This pattern is most commonly seen after chlorpromazine and amiodarone (slate grey pigmentation)

Non-medical update

- Minor surgery or other invasive procedures for people taking novel oral anticoagulants (NOACs): dentists and others who perform minor procedures, eg administer joint injections have criteria to assess suitability for those patients taking warfarin. Recent information has been presented to the NMP podiatry forum on the relevance of concomitant treatment with NOACs. This covers issues such as timing of next dose, effect of renal impairment on timings. Specific advice for [apixaban](#), [dabigatran](#) and [rivaroxaban](#) can be found on Staffnet.
- The new absorbent dressing of choice in all care settings in NHSGGC is now Premierpore instead of Mepore; with supplies available in wholesalers. Community pharmacists have been notified to run down current stock of Mepore.

PostScript Extra: NSAIDs

There is a new PostScript Extra bulletin on Oral NSAIDs available [here](#). This is an update to the previous version and is in line with the new anti-inflammatory guideline on nonsteroidal oral medicines which will shortly be posted on StaffNet. Naproxen and ibuprofen are the oral NSAIDs of choice taking into consideration the patient's GI and cardiovascular risks. The lowest effective dose should be used to control the patient's symptoms for the shortest duration possible.

ADTC decisions summary

See the [website](#) for full list of medicines and details of indications and restrictions.

The following medicines were added to the *Adult Total Formulary*:

- **Canagliflozin tablets (Invokana[®])** for use in adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control as add-on therapy, when these, together with diet and exercise, do not provide adequate glycaemic control. It is restricted to initiation by clinicians experienced in the management of diabetes.
- **Fluticasone furoate and vilanterol dry powder inhaler (Relvar Ellipta[®])** for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta2-agonist and inhaled corticosteroid) is appropriate in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonists is included in the GGC Adult Formulary for the indication in question.

Prescribing note: Fluticasone furoate is a high-potency inhaled steroid (with a dose of 92micrograms once daily broadly equivalent to 250micrograms twice daily of fluticasone propionate). When used for asthma, due consideration for the likelihood of step-down should be given prior to initiation as there are no available step-down options containing a dose lower than 92 microgram of fluticasone furoate.

Other *Formulary* decisions

- **Diprobase[®] cream** for the use as an emollient for dry skin conditions has been moved to the Total Formulary. Zerobase[®] Cream is the nearest Preferred List option.



www.ggcprescribing.org.uk

Contact us:

postscript@ggc.scot.nhs.uk

0141 201 5348