NHS North of Tyne

Clinical Guidelines

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Newcastle, North Tyneside and Northumberland Guidelines on Antiplatelet Therapy

Ratified by:	NHS North of Tyne Commissioning Integrated Governance Committee
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Organisations signed up to this guideline:	NHS North of Tyne (on behalf of the PCT's), Newcastle upon Tyne Hospitals NHS Foundation Trust, Northumbria Healthcare Foundation Trust
Name of originator/author:	Glyn Trueman
Target audience:	All clinicians in the Newcastle, North Tyneside and Northumberland areas involved in the management of antiplatelet therapy
Consultation Process:	Guideline group was multidisciplinary from all representative organisations
Mandatory/Statutory Standards or Requirements	Standards for Better Health NHS Litigation Authority Standards

	QOF targets
Training Requirements	No specific training requirements
Distribution	Primary care, secondary care
Implementation	Implementation process in primary care required. Distributed to GPs and uploaded onto infonet.
Monitoring Compliance	QOF targets, audit from part of QIG.

North of Tyne
Antiplatelet Guidelines

These notes are intended to give information and guidance on the appropriate use of aspirin, clopidogrel and dipyridamole in the prevention of atherosclerotic cardiovascular events. They should be used with the separate supporting information and prescribing information in the BNF.

1. Primary Prevention

Aspirin is not licensed for the primary prevention of vascular events. If aspirin is used in primary prevention, the balance of benefits and risks should be considered for each individual, particularly the presence of risk factors for vascular disease (including conditions such as diabetes) and the risk of gastrointestinal bleeding[1]

A. Prophylaxis of Cardiovascular Disease

Consider use of dispersible aspirin 75 mg daily[2] in

1. People with Type 1 and Type 2 diabetes

- With microalbuminuria / proteinuria.
- With other vascular risk factors, particularly those with multiple risk factors, and in people aged 50 years and over. Risk factors include treated hypertension, overweight / obesity / metabolic syndrome, current or recent smoker, high risk lipid profile, family history of premature coronary disease (particularly of acute MI, CABG, sudden coronary death).

2. High risk people without symptomatic or prior occlusive vascular disease and without diabetes

- With a 10 year cardiovascular disease risk of 20% or more, particularly those at higher levels of risk, and in those with more vascular risk factors. Risk factors include treated hypertension, overweight / obesity / metabolic syndrome, current or recent smoker, high risk lipid profile, family history of premature coronary disease (particularly of acute MI, CABG, sudden coronary death).

In all people treated with aspirin for primary prevention

- Patients currently treated with aspirin for primary prevention who are tolerating this should continue, providing there are no contra-indications.
- In all cases the blood pressure should be controlled to < 150/90 mmHg before aspirin is started for primary prevention.
- If patients are treated with aspirin for primary prevention and develop uncontrolled hypertension, with a sustained BP > 150/90 mmHg, aspirin should be temporarily withheld until the blood pressure is controlled.
- High risk patients intolerant of other preventative treatment such as statins may have more to gain, and be more likely to be considered for aspirin.
- In all patients the balance of benefit and risk should be considered. Frailty, co-morbidities and treatment with other drugs such as steroids and NSAIDs are all associated with an increased risk of bleeding, for example.

CLOPIDOGREL[3] IS NOT INDICATED FOR USE IN THE PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE

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[1] MHRA Drug Safety Update: Volume 3 Issue 3, October 2009 (162Kb)

[2] Use of enteric coated tablets is not recommended.

[3] Also applies to dipyridamole and antiplatelet drugs other than aspirin

B Atrial fibrillation

Aspirin dispersible 75 mg (to 300 mg) daily indefinitely

Aspirin is less effective than warfarin, but may be used in patients where the use of anticoagulants is inappropriate or if the risk of stroke is low (e.g. patient under 65 with no other risk factors for stroke).

Clopidogrel 75 mg daily may be considered in those patients where antiplatelet rather than anticoagulant therapy is appropriate and aspirin cannot be used (unlicensed) – See Atrial fibrillation guidelines.

2. Secondary Prevention of CHD and Stroke

Antiplatelet therapy is indicated for life in all patients with a diagnosis of:

- Ischaemic heart disease
- Ischaemic stroke or TIA
- Peripheral artery disease

(Unless they develop an indication for anticoagulation)

1st Choice – dispersible ***Aspirin 75 mg daily***
(use of enteric coated aspirin is not recommended)

2nd Choice – ***Clopidogrel 75 mg daily*** **only** if aspirin is contraindicated or not tolerated despite the adoption of measures to improve tolerability – see notes on **aspirin** (section 3)

Combination Antiplatelet Regimens

Indication	Treatment	Notes
	Aspirin dispersible **75 mg daily indefinitely +**	
Myocardial Infarction with ST- segment-elevation (STEMI) - Patients presenting within 12 hours of acute infarction, excluding those at increased risk of bleeding	***Clopidogrel 75 mg daily*** *for 12 months then review** [4], irrespective of whether the patient receives primary PCI and is fitted with a stent or not	*Aspirin* loading dose 300 mg[5] *Clopidogrel* loading dose - primary PCI 600 mg (patients undergoing thrombo-lysis with no PCI: if ≤ 75yrs 300 mg loading dose, if > 75 yrs - no loading dose)
Acute Coronary Syndrome Patients with Non ST-segment-elevation (NSTEMI) (includes unstable angina)	***Clopidogrel 75 mg daily*** *for 12 months then review** [2]	*Aspirin* loading dose 300 mg *Clopidogrel* loading dose - 600 mg if undergoing PCI within 24 hours, otherwise 300 mg
Stable Elective PCI Patients		
Bare Metal Stent fitted	***Clopidogrel 75 mg daily*** *for 1 month* (up to 12 months on cardiologist advice)	
Drug Eluting Stent fitted	***Clopidogrel 75 mg daily*** *for 12 months then review**	*Clopidogrel* 600 mg loading dose given 2 hours before PCI
PCI procedure to left main stem coronary artery	***Clopidogrel 75 mg daily***, *lifelong unless advised by cardiologist*	
Carotid Artery Stenting	***Clopidogrel 75 mg daily*** *for 4 weeks following procedure*	*Clopidogrel* 75 mg daily usually for 7 days before procedure
Ischaemic Stroke and TIA	***Dipyridamole*** *200 mg MR bd for at least 2 years if tolerated*	Monotherapy with clopidogrel should be considered in those who do not tolerate aspirin
N.B. When a planned Stop/ Review Date for clopidogrel is reached, the patient should be reviewed and treatment stopped, unless there is good reason for continuing, e.g. If the patient has had a later cardiovascular event/intervention for which clopidogrel is indicated. *** The review should normally be carried out by the clinician responsible for prescribing the**		

[4] In patients fitted with drug eluting stents clopidogrel treatment should be reviewed after 12 months, longer term use may be advised taking into account the risk for further events.

[5] 300 mg orally should be given as soon as possible to all suspected MI patients. The tablets should be chewed then swallowed - usually given by paramedics prior to hospital admission)

clopidogrel (usually the GP, taking into account patient specific advice from hospital specialists).

3. Aspirin

USE: First choice antiplatelet drug for the:

- Primary prevention of coronary heart disease/strokes in patients at high risk.
- Secondary prevention of thrombotic events in patients with ischaemic heart disease, ischaemic stroke or TIA and peripheral artery disease.

DOSE: Usually 75 mg daily for prophylaxis, unless otherwise specified by consultant.
FORMULATION: 75 mg dispersible tablets. Use of enteric coated tablets is not recommended.

Gastrointestinal (GI) Symptoms - Use of Aspirin
Patients treated with aspirin who develop dyspepsia
If troublesome try/consider these options:

- **Review and modify other contributory factors and medication (including purchased medicines), which may also be causing dyspeptic symptoms** e.g. excess alcohol intake, non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids
- Taking aspirin with food
- Reducing aspirin dose to 75 mg (if taking more)
- Using aspirin in combination with an antacid or acid suppressant (e.g. a proton pump inhibitor [PPI] such as omeprazole 20 mg, or lansoprazole 15 mg-30 mg). If aspirin being used for primary prevention individual assessment and discussion with the patient, about whether to stop aspirin or to continue in combination with a PPI

If all the above fail, consider using clopidogrel instead of aspirin for secondary prevention only. Clopidogrel is not indicated for primary prevention and if PPI treatment has been prescribed to control aspirin induced dyspepsia it should be stopped[6].

Enteric coated aspirin does NOT reduce GI symptoms – its use is not recommended.

Indications for further investigation should be informed by guidelines for management of dyspepsia.

History of gastrointestinal bleeding with aspirin or a NSAID - Aspirin plus a proton pump inhibitor e.g. lansoprazole 30 mg daily. Much safer than using clopidogrel, if ulcer is known to be healed. If patient is H. pylori positive, eradication is advised.

History of peptic ulcer - May be used with caution, consider use with proton pump inhibitor.

Hypersensitivity to aspirin or NSAIDs (bronchospasm, rash etc.)
Avoid aspirin - consider clopidogrel (for secondary prevention only).

4. Clopidogrel

USES: Alternative to aspirin for the secondary prevention of atherosclerotic events in:

- Patients with a genuine allergy to aspirin.
- Patients who develop troublesome dyspepsia with aspirin where this cannot be controlled/ prevented by the measures recommended above.
- **Use aspirin + a PPI if a history of clinically important acute or chronic gastro-intestinal haemorrhage caused by aspirin or NSAIDs**.
- **PPIs should not be used in those taking clopidogrel unless use is considered essential**[6].

[6] The MHRA and EMEA have advised that proton pump inhibitors (PPIs) should only be used in patients taking clopidogrel where their concomitant use is considered essential. Evidence from several studies to indicates that some PPIs might interact with clopidogrel reducing its effectiveness and increasing the risk of thrombotic events.

- Clopidogrel is not licensed for primary prevention.
- Prescriptions, letters etc from clinicians should clearly indicate the reason for using clopidogrel and the planned duration of treatment by stating a stop/review date (if it is intended that treatment is lifelong, this should be made clear).

AVOID BOTH ASPIRIN AND CLOPIDOGREL IN PATIENTS WITH BLEEDING DISORDERS OR ACTIVE PEPTIC ULCER. ONLY USE IN PATIENTS WITH A HISTORY OF RECENT MAJOR GASTRO-INTESTINAL OR INTRACRANIAL BLEED AFTER A CAREFUL ASSESSMENT OF RISK .

5. Dipyridamole

USE: In combination with aspirin for the secondary prevention of ischaemic stroke and TIAs.

DOSE: 200 mg (modified release capsules) twice daily.

- Poorly tolerated, commonly causes side effects such as gastro-intestinal effects, dizziness, myalgia, throbbing headache, hypotension, hot flushes and tachycardia.
- Use in combination with aspirin is recommended by NICE. Treatment is advised for at least 2 years and may be continued indefinitely - ESPIRIT study indicates benefit for at least 5 years.
- Because of tolerability problems, some clinicians limit its use to those patients who are at higher risk of recurrent stroke/ TIA and those who have recurrent events whilst taking aspirin.
- Not considered effective in preventing cardiac events.
- Clopidogrel has similar efficacy to aspirin + dipyridamole and is more effective than dipyridamole monotherapy. It should therefore be used in those who cannot take aspirin.

6. Antiplatelet Drugs and Surgery

- Aspirin and clopidogrel increase bleeding associated with surgery.
- The risks from excess bleeding must be balanced against the increased risk of a thromboembolic event if antiplatelet drugs stopped (some evidence of a rebound effect).

MINOR SURGERY

Antiplatelet therapy **does not need to be withdrawn** from patients undergoing minor surgery, where bleeding can be easily managed or where the risk of bleeding is low e.g.

a) Dental surgery including fillings and tooth extractions in the community
b) Skin excisions including biopsies and Mohs procedures
c) Cataract Surgery

- Be aware of the increased risk of bleeding and be prepared to cope e.g. by using topical haemostatic agents when necessary.
- Time procedures so that any bleeding problems during or after procedure are easier to deal with.

ENDOSCOPY PATIENTS - The management of aspirin and clopidogrel use in patients undergoing endoscopic procedures is based on the relative risks of the procedure and underlying condition – see local guidelines. Patients who need GI endoscopy should only be referred for open access tests if clopidogrel can be safely stopped 7 days before procedure (aspirin is continued).

MAJOR ELECTIVE SURGERY

The decision to stop treatment with clopidogrel and/or aspirin prior to major elective surgery should be based on a careful assessment of the patient's risk from increased bleeding vs. the increased risk of a thrombotic event. If appropriate provide short term cover with other agents (e.g. heparin) and restart antiplatelet therapy as soon as possible after surgery. In those on combination antiplatelet therapy it may only be necessary to stop the clopidogrel.

- Clopidogrel is more likely than aspirin to cause clinically significant bleeding problems.

- Specialist advice should be sought in high-risk patients, especially those fitted with stents & those taking both clopidogrel & aspirin. Stopping antiplatelet drugs can increase the risk of thrombotic events. In some the advice may be to stop clopidogrel, but not aspirin.
- Clopidogrel should normally be stopped 5 days before CABG.
- If antiplatelet therapy is to be withdrawn, it is usual to stop clopidogrel 7 days before major surgery and, where necessary, aspirin at least 5 to 7 days before the surgery.

7. Use of Aspirin and Clopidogrel with Anticoagulants

The concomitant use of anticoagulants, e.g. warfarin, with aspirin and/or clopidogrel increases the risk of bleeding. Such combinations should only be initiated in secondary care and they should not be used in the community unless specifically advised by a hospital consultant.

8. Use of Aspirin and Clopidogrel with NSAIDs

The use of aspirin and/or clopidogrel in combination with an NSAID increases the risk of gastro-intestinal bleeding. If such combinations cannot be avoided, they may be used with caution in patients where simple analgesia (e.g. with paracetamol) is inadequate.