CHAPTER 2 CARDIOVASCULAR SYSTEM

2.1 Acute stroke

NICE CG68 - Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA), July 2008 and NICE TA 210 - Vascular disease clopidogrel and dipyridamole, December 2010

Acute ischaemic stroke patients should be assessed for thrombolytic therapy. If they fulfil inclusion criteria a Neurology Registrar or the Stroke Team (working hours, bleep 6432, switchboard out of hours) should be informed as soon as possible. For inclusion and exclusion criteria, as well as control of blood pressure before thrombolysis for acute ischaemic stroke, please refer to the thrombolysis pathway which is available in the Emergency Unit at UHW.

Examination at presentation should describe the neurological impairments and identify the stroke sub-type. Assessment of consciousness and swallowing should always be recorded. Swallow must always be assessed to avoid risk of aspiration. If in doubt keep nil by mouth and maintain hydration by IV fluids until patient assessed by Speech and Language Therapist or other trained staff. Nutritional supplementation by NG tube or PEG may have to be considered.

Note: Presence of gag reflex does not mean that the swallow is safe.

All acute stroke patients must be transferred to the Acute Stroke Unit within 4 hours of admission

- General measures: maintain adequate nutrition, care for pressure areas and monitor bladder and bowel function.

- All acute ischaemic stroke patients should receive aspirin 300mg stat as soon as possible and aspirin 300mg od for fourteen days; on day 15 aspirin should then be discontinued and clopidogrel 75mg od, long term, should be prescribed first-line for secondary prevention (please see section 2.2 for further details including secondary prevention in patients who have had a suspected TIA). Aspirin can be given by NG tube or rectally for those who are unable to swallow. Note: haemorrhagic infarction is not a contraindication for aspirin.

- Patients at a particularly high risk of early DVT (e.g. those with a history of previous DVT, complete paralysis of the leg, known thrombophilia or active cancer, or who are current or recent smokers) can be given prophylactic heparin, in a low dose regimen (e.g. enoxaparin 40mg once a day).

- Anti-embolism stockings should not be used for DVT prevention in stroke patients as they are ineffective.

- In people with prosthetic valves who have disabling cerebral infarction and who are at significant risk of haemorrhagic transformation, anticoagulation treatment should be stopped for 1 week and aspirin 300mg daily substituted.

- People with disabling ischaemic stroke who are in atrial fibrillation should be treated with aspirin 300mg daily for the first 2 weeks before considering anticoagulation treatment.

- People with ischaemic stroke and symptomatic proximal DVT or PE should receive anticoagulation treatment in preference to treatment with aspirin unless there are other contraindications to anticoagulation. Inferior vena cava filters
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should be considered in patients with intracerebral haemorrhage and those who have very high risk of intracranial bleeding.

2.2 Secondary prevention

- Patients with ischaemic stroke should receive long term clopidogrel 75mg od (on its own unless there are indications for dual treatment with aspirin e.g. patients with coronary artery stents and in those with recent history of non-ST elevation acute coronary syndrome)
- Patients who have had a suspected TIA should receive long term clopidogrel 75mg od (unlicensed use)
- Stroke/TIA patients unable to tolerate clopidogrel, or in whom it is contraindicated, should receive modified release (MR) dipyridamole 200mg bd and aspirin 75mg od. If both clopidogrel and aspirin are contraindicated or not tolerated then MR dipyridamole alone is recommended.
- Prescribe aspirin dispersible not enteric coated. There is no evidence that there is less GI ulceration with enteric coated aspirin. If patients complain of dyspepsia with dispersible aspirin ensure that it is taken with food or milk.
- Consider warfarin or other oral anticoagulants, if appropriate, in cardioembolic ischaemic strokes secondary to atrial fibrillation (aim for target INR 2.5). Anticoagulation should be started as soon as possible in patients with minor stroke or TIs. In patients with severe stroke the risk/benefit of anticoagulation should be assessed and, if appropriate, commenced after 2 weeks. Anticoagulants should not be used for patients in sinus rhythm unless there is a reason to suspect cardiogenic embolism.
- Hypertension – record BP at least twice a day. Defer reduction in BP for 14 days, unless there is a hypertensive emergency with one or more of the following:- hypertensive encephalopathy, acute dissection, hypertensive cardiac failure/myocardial infarction, hypertensive nephropathy, pre-eclampsia/eclampsia, intracerebral haemorrhage with systolic BP over 200mmHg.
- Blood pressure should be lowered to between 120–130mmHg systolic and 70-80mmHg diastolic.
- Therapy with a statin should be considered for all patients following ischaemic stroke to lower total cholesterol to <4 mmol/L or by 25% (whichever is greater).
- All patients who smoke should be advised to stop smoking.
- In patients with diabetes HbA1c should be maintained within normal range (26-48 mmol/mol)
- Patients with ipsilateral symptomatic carotid stenosis of greater than 70% should be considered for carotid endarterectomy as soon as possible, ideally within 2 weeks. All patients should be assessed for other vascular risk factors and be treated or advised appropriately.
- All stroke patients should be assessed for transfer to the Stroke Rehabilitation Unit.
2.3 Heart failure

NICE CG108 – Chronic heart failure, August 2010

- Establish presence of left ventricular systolic dysfunction. Treatment of diastolic dysfunction remains controversial.

- Identify and treat underlying cause and triggers for decompensation (e.g. ischaemia, anaemia, thyrotoxicosis, valve disease, hypertension)

- Review concurrent medications. Some treatments can aggravate heart failure (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), steroids, glitazones, negative inotropes).

- Offer both an ACE inhibitor (ACE-I) and a beta blocker licensed for heart failure to all patients with heart failure due to left ventricular systolic dysfunction. Use clinical judgement when deciding which drug to start first, but ensure that patients are established on both neurohormonal blocking agents.

- Add an aldosterone antagonist to patients with ejection fraction (EF) <35% remaining symptomatic (NYHA II-IV) after ACE-I and beta blocker established at optimal doses. (See section 2.3.6)

- Ivabradine may be considered in patients with heart failure and heart rate >75bpm in whom beta blockers are contraindicated or not tolerated.

- Monitor electrolytes regularly; especially in patients treated with multiple neurohormonal blocking agents.

- For patients remaining severely symptomatic (NYHA III/IV) despite optimal medical therapy, EF <35%, and sinus rhythm with bundle branch block (QRS > 120msec) on resting ECG; consider referral for cardiac resynchronisation therapy (biventricular pacing).

- Patients with post-MI left ventricular systolic dysfunction (EF <30%) and QRS >120msec are at high risk of sudden cardiac death and require urgent evaluation for defibrillator therapy.

2.3.1 Loop and thiazide diuretics for heart failure

- Loop diuretics are useful for peripheral oedema and/or breathlessness; there is no reliable prognostic benefit. Emphasis should generally be on high dose ACE-I with low dose diuretic. In severe end stage heart failure, metolazone or bendroflumethazide (2.5-5mg 2/3 times a week) may be added to loop diuretics to produce an aggressive diuresis; but this needs careful monitoring (hypotension, hyponatraemia, uraemia).

2.3.2 Angiotensin Converting Enzyme Inhibitors (ACE-I) for heart failure

- An ACE-I should be considered as the first line agent to block the renin-angiotensin axis for all patients with left ventricular systolic dysfunction, irrespective of aetiology and symptoms.
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- Initiate ACE-I and titrate up to doses used in clinical trials unless symptomatic hypotension and/or renal dysfunction occurs.

- Consider reducing loop diuretic dose if patient is taking more than 40mg furosemide daily (if clinical symptoms allow) or if volume depleted (postural hypotension, dry tongue or skin, poor skin turgor, increased creatinine and electrolytes).

- Stop potassium sparing combination diuretics e.g. change co-amilofruse to furosemide.

- Measure baseline electrolytes, eGFR, and creatinine prior to ACE-I initiation. Repeat 7-10 days later and one week after each dose increase.

- Start with a small dose and titrate upwards over the next few days (in-patient) or weeks (out-patient).

- For the treatment of heart failure increase the dose to the maximum tolerated or the target dose (see table), not according to symptomatic response.

<table>
<thead>
<tr>
<th></th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>lisinopril</td>
<td>2.5-5mg od</td>
<td>30-35mg od</td>
</tr>
<tr>
<td>ramipril</td>
<td>2.5mg od</td>
<td>5mg bd or 10mg od</td>
</tr>
</tbody>
</table>

2.3.3 Beta-blockers for heart failure

- Offer beta-blockers licensed for heart failure to all patients with heart failure due to left ventricular systolic dysfunction, including older patients and patients with peripheral vascular disease, erectile dysfunction, diabetes mellitus, interstitial pulmonary disease and COPD without reversibility.

- Check ECG to exclude heart block (left bundle branch block is not a contraindication to beta-blocker therapy in heart failure).

- Start with low dose and titrate with assessment of heart rate, blood pressure, ECG and clinical status (symptoms, signs, especially signs of congestion, body weight) after each titration. Check blood electrolytes, eGFR, and creatinine 1-2 weeks after initiation and 1-2 weeks after final dose titration.

- Patients who are already being treated with a beta-blocker (not licensed for heart failure) for a concomitant condition (e.g. for angina, hypertension) should continue with that beta-blocker unless their symptoms deteriorate. In these cases, the beta blocker should be switched to one that is licensed for use in heart failure.

<table>
<thead>
<tr>
<th>Beta Blockers for heart failure</th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>bisoprolol</td>
<td>1.25mg od</td>
<td>10mg od</td>
</tr>
<tr>
<td>carvedilol</td>
<td>3.125mg bd</td>
<td>25mg bd*</td>
</tr>
<tr>
<td>nebivolol</td>
<td>1.25mg od</td>
<td>10mg od</td>
</tr>
</tbody>
</table>

*Note: target dose of carvedilol is 50mg bd if patient weight is >65kg
2.3.4 Beta-blockers problem solving

- Worsening symptoms
  - Congestion: double dose of diuretic, or halve dose of beta-blocker
  - Fatigue: halve dose of beta-blocker

- Bradycardia
  - Review need for other negatively chronotropic medications (e.g. diltiazem, digoxin, amiodarone)
  - If heart rate <50bpm with worsening symptoms: halve dose of beta-blocker.
  - ECG to exclude heart block

- Hypotension
  - Asymptomatic: no change in treatment usually required.
  - Symptomatic: review need for other hypotensive medication. If no signs of congestion, halve dose of diuretic.

NB: avoid stopping beta-blockers suddenly due to risks of rebound tachycardia, ischaemia, and arrhythmias.

2.3.5 Heart rate lowering in heart failure

Consider additional heart rate lowering with ivabradine in patients with sinus rhythm, resting heart rate >75bpm, EF <35%, and NYHA II-IV symptoms despite optimal beta-blocker, ACE-I, and aldosterone antagonist therapy.

2.3.6 Aldosterone antagonists in heart failure

- Additional neurohormonal blockade with aldosterone antagonists should be considered once ACE-I and beta blocker therapies have been established.

- Monitor electrolytes, eGFR and creatinine 1 week after initiation and 1-2 weeks after each dose titration. Aldosterone antagonist/ACE-I combination therapy can cause severe electrolyte abnormalities in up to 10% of patients. If hyperkalaemia occurs, halve the aldosterone antagonist dose and recheck biochemistry.

- Spironolactone should be considered in chronic heart failure (NYHA III/IV) and EF <35%. Starting dose is 12.5mg to 25mg daily, with appropriate monitoring. Up to 50mg daily may be used if advised by a specialist and there are no problems with hyperkalaemia or impaired renal function.

- Eplerenone may be considered in stable patients with symptomatic heart failure and EF ≤40%, following myocardial infarction (start treatment within 3-14 days of event).

- Eplerenone may be considered as an alternative aldosterone antagonist in symptomatic chronic heart failure patients if progestational and antiandrogenic side effects of spironolactone prohibit its use.
2.3.7 ACE-I, Angiotensin-II Receptor Antagonists (A-II RAs) problem solving

- Hypotension
  - Asymptomatic: does not usually require any change in treatment.
  - Symptomatic: consider reducing diuretic dose, and/or reducing doses of other hypotensive agents.
- Worsening renal function
  - A small, asymptomatic increase in creatinine is common (up to 50% increase of creatinine above baseline, or 200mmol/L; whichever is the smaller).
  - Rise in serum potassium up to 5.9mmol/L is also acceptable.
  - If potassium rises >6.0mmol/L, or creatinine increases by >100% or to >350 mmol/L, stop ACE I/A-II RA/aldosterone antagonist and seek specialist advice.

2.3.8 Second line treatments for heart failure

Seek specialist advice before offering second-line treatment to patients with heart failure due to left ventricular systolic dysfunction.

Seek specialist assessment of patients with QRS >120mec for device therapies.

2.3.9 Angiotensin-II Receptor Antagonists (A-II RAs)

- Only losartan, candesartan and valsartan are licensed in heart failure.
- ACE-I intolerance is rare (<10%)
- A-II RAs may be used with caution in patients with a history of ACE-I-related angioedema.
- Combination candesartan/ACEI or valsartan/ACEI (post-MI heart failure) may be useful in some patients. Specialist advice and frequent haemodynamic and biochemical monitoring is recommended.

2.3.10 Digoxin in heart failure

- For heart failure patients in atrial fibrillation, heart rate should be optimised first line with beta blockers. Consider adding in digoxin for additional heart rate control if rate control is sub-optimal or increased dose of beta blockers not tolerated.
- Use digoxin first line in patients with atrial fibrillation and any degree of heart failure.
- Add digoxin if a patient in sinus rhythm remains symptomatic with frequent hospitalisations despite optimal first line treatment for heart failure.

2.3.11 Combination treatment with hydralazine/nitrates

- This combination may be considered if a patient remains symptomatic despite optimal therapy with an ACEI and a beta-blocker (especially if the patient is of African or Caribbean origin and has moderate to severe heart failure (NYHA class III–IV).
- Combination treatment with hydralazine/nitrates may be considered in patients intolerant of ACEI and/or A-II RAs.
2.3.12 Amiodarone

- Amiodarone does not prevent sudden arrhythmic death in heart failure; consider referral for an implantable defibrillator.

2.3.13 Anticoagulation

- Anticoagulation is indicated in presence of AF.
- In patients with heart failure and sinus rhythm, consider anticoagulation for those with a history of thromboembolism, left ventricular aneurysm or intra-cardiac thrombus.

2.3.14 Statins

- Statins should be stopped in heart failure patients with non-significant coronary artery disease (i.e. not the cause of heart failure), unless otherwise indicated: e.g. high risk primary prevention.

2.3.15 Aspirin

- Aspirin should be stopped in heart failure patients with non-significant coronary artery disease (i.e. not the cause of heart failure), unless otherwise indicated: e.g. high risk primary prevention.

2.3.16 Calcium channel blockers

- Amlodipine may be considered for the treatment of hypertension and/or angina in patients with heart failure but verapamil, diltiazem or short-acting dihydropyridine agents should be avoided.

2.3.17 Vaccinations

- Patients with heart failure should be offered an annual vaccination against influenza and a one off vaccination against pneumococcal disease.

2.4 ST-segment elevation myocardial infarction

*NICE CG167: Myocardial infarction with ST-segment elevation, July 2013*

**Default treatment of choice is primary percutaneous coronary intervention (PCI).** This is the preferred coronary reperfusion strategy for people with acute STEMI if:

- presentation is within 12 hours of onset of symptoms **and**
- primary PCI can be delivered within 120 minutes of the time when fibrinolysis could have been given.

Consider coronary angiography, with follow-on primary PCI if indicated, for people with acute STEMI presenting more than 12 hours after onset of symptoms if there is evidence of continuing myocardial ischaemia.
2.5 Aspirin and prasugrel in acute myocardial infarction

- Aspirin 300mg stat. and then 75mg daily as long term maintenance dose and prasugrel 60mg stat and then 10mg daily for 12 months should be given to all patients with STEMI undergoing primary PCI.
- Maintenance dose prasugrel should not be used in patients under 60kg or over 75 years of age. These patients (STEMI and Primary PCI) should receive aspirin as above. They should also be given a maintenance dose of clopidogrel 75mg daily for one month (Bare Metal Stent) or for 12 months (Drug Eluting Stent).

2.6 Unstable angina and non Q-wave myocardial infarction (non-ST elevation acute coronary syndromes)

NICE CG 94 - Unstable angina and NSTEMI, March 2010

- Patients are best managed on the Coronary Care Unit.
- Beta-blocker (e.g. bisoprolol 5mg orally) to prevent tachycardia. Aim for a resting heart rate of 55-70. Patients unable to tolerate a beta-blocker should be given a "rate-limiting" calcium antagonist e.g. diltiazem (orally).
- Fondaparinux 2.5mg SC once daily (duration depends on a patient’s clinical progress but should not exceed 8 days).
- Isosorbide dinitrate 2mg/hour IV initially, titrated against blood pressure and clinical response.
- Aspirin 300mg stat and 75mg od (orally). For patients with true aspirin hypersensitivity give clopidogrel monotherapy (600mg stat and 75mg od).
- Clopidogrel 600mg loading dose in addition to aspirin in all patients with a predicted 6-month mortality of more than 1.5% and no contraindications (for example, an excessive bleeding risk).
- Clopidogrel 600mg stat and then 75mg daily is currently continued in combination with low dose aspirin for 12 months after the most recent acute episode of troponin positive non-ST-segment-elevation ACS.
- After this period, provided no further acute coronary event has occurred, clopidogrel can be stopped. If clopidogrel is initiated it is essential that the GP is informed of the indication and intended duration of treatment via the TTH.
- High risk patients with NSTEMI (or STEMI) may be prescribed prasugrel or ticagrelor at the operator’s discretion.

Fondaparinux

- There is no known antidote to fondaparinux.
- Treatment with any anticoagulant may unmask lesions which result in unexpected bleeding. In such circumstances fondaparinux should be discontinued and the cause of bleeding identified and arrested. If necessary, blood product support should be initiated, with transfusion of red cells, fresh frozen plasma and platelets, based on the clinical picture and laboratory results. If bleeding continues contact haematology for advice.
- Fondaparinux should not be used in patients with creatinine clearance < 30 mL/min. In such patients enoxaparin 1mg/kg daily is recommended.
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- Overlapping of anti-thrombin agents is associated with an increased risk of bleeding. Therefore in cases where the need arises for a change in the anticoagulant agent, treatment stacking should be avoided. For example in a patient previously treated with fondaparinux, the first dose of enoxaparin (or UFH) should be given 24 hours after the last dose of fondaparinux. Conversely, in a patient previously treated with enoxaparin on a twice daily basis the first dose of fondaparinux (or UFH) should be given 12-hours after the last dose of enoxaparin.

2.7 Percutaneous Coronary Intervention (PCI)

- Clopidogrel 600mg stat at least 2 hours before PCI, then 75mg od for 4 weeks (after implantation of a bare metal stent) or for 12 months (after implantation of a drug-eluting stent), in combination with aspirin 75mg.
- Clopidogrel/prasugrel/ticagrelor should be continued for 12 months in a troponin positive non-ST-segment elevation ACS (after implantation of a bare metal stent).

2.8 Warfarin and anti-platelet therapy

Concomitant therapy needs to be assessed on a case by case basis by a Consultant cardiologist. The situation usually arises where a patient is on warfarin for a prior condition and then undergoes intracoronary stenting. Please discuss with a senior colleague.
2.9 MI: Secondary prevention

NICE CG 172, MI – secondary prevention, November 2013

All patients who have had an acute MI should be given advice on lifestyle changes, e.g. exercise, alcohol intake, diet, smoking cessation and offered treatment with a combination of the following drugs.

- **ACEI** (or an angiotensin receptor blocker (A-II RA) if the patient is intolerant to ACEIs) titrated to target or maximum tolerated dose and continued indefinitely in patients with preserved LV function or with left ventricular systolic dysfunction, whether or not they have symptoms of heart failure (likewise for patients who have had a proven MI in the past i.e. more than one year ago). Doses should be titrated upwards at short intervals (for example every 12-24 hours) until the maximum tolerated or target dose is reached. If it is not possible to complete the titration during the patient’s hospital admission, it should be completed within 4-6 weeks of hospital discharge.

- **beta-blocker** – titrated up to the maximum tolerated or target dose and continued indefinitely in all patients with LVSD and for at least 12 months in patients without LVSD (likewise for patients who have had an MI more than one year ago who have LVSD).

- Consider diltiazem or verapamil in patients without pulmonary congestion if beta-blocker contraindicated or not tolerated and ejection fraction is >40% (if S/R preparation prescribe as brand name). Ivabradine may also be considered in beta-blocker intolerant patients - seek cardiologist advice.

- **aspirin** (or clopidogrel for patients with aspirin hypersensitivity) – continued indefinitely unless there is an indication for anticoagulation (likewise for patients who have had an MI more than one year ago).

- For an ST-segment-elevation MI (not treated with primary PCI) initiate (during the first 24 hours after the MI) clopidogrel 600mg stat (in patients less than 75 years of age) and then 75mg od (in combination with aspirin, 300mg stat and then 75mg od) for four weeks and then revert back to aspirin monotherapy. CG 172 - offer clopidogrel as a treatment option for at least a month and consider continuing for up to 12 months to patients who have had a STEMI and medical mananagement with or without reperfusion treatment with a fibrinolytic agent.

- For a ST-segment-elevation MI treated with primary PCI initiate prasugrel 60mg stat and then 10mg od (in combination with aspirin, 300mg stat and then 75mg od) for 12 months and then revert back to aspirin monotherapy*

- CG 172 - For a STEMI in patients who have received a bare-metal or drug-eluting stent offer dual anti-platelet therapy as a treatment option for up to 12 months.
CG 172 - continue the second antiplatelet for up to 12 months in people who have had a STEMI and who received coronary artery bypass graft (CABG) surgery.

- Treat with clopidogrel in combination with low-dose aspirin for 12 months after the most recent episode of non-ST-segment-elevation acute coronary syndrome and then continue with aspirin 75mg od* unless there are indications to continue dual anti-platelet therapy.

- Patients who complain of dyspepsia with aspirin should be co-prescribed a proton pump inhibitor rather than switched to clopidogrel.

- Patients who also have other clinical vascular disease should be offered clopidogrel instead of aspirin (NICE TA210) when they have:  
  - had an MI and stopped dual antiplatelet therapy or  
  - had an MI more than 12 months ago

**Antiplatelet therapy in people with an indication for anticoagulation**

- For patients who have had an MI and also have an indication for anticoagulation, consider bleeding, thromboembolic and cardiovascular risks.

  - Unless there is a high risk of bleeding, continue anticoagulation and add aspirin (or clopidogrel in patients with a sensitivity to aspirin) to treatment in patients who:
    - have had their condition managed medically or
    - have undergone balloon angioplasty or
    - have undergone CABG surgery

- Continue anticoagulation and add clopidogrel (but no aspirin) to treatment in people who have had an MI and undergone PCI.

- Do not routinely offer warfarin in combination with prasugrel or ticagrelor to people who need anticoagulation who have had a MI.

- After 12 months post MI continue anticoagulant and assess the need for ongoing antiplatelet therapy taking into account the indication for the anticoagulant, thromboembolic, bleeding and cardiovascular risks and the wishes of the patient.

- Do not add new oral anticoagulant (rivaroxaban, apixaban or dabigatran) in combination with dual antiplatelet therapy in patients who have had an MI.

- Consider using warfarin and discontinuing treatment with a new oral anticoagulant in people who otherwise need anticoagulation and who have had an MI.

- **Statin** - all patients should be offered treatment as soon as possible after an MI.
Aldosterone antagonists

- Initiate an aldosterone antagonist licensed for post-MI treatment i.e. eplerenone within 3-14 days of the MI (preferably after ACEI therapy) for patients who have symptoms and/or signs of heart failure and LVSD. Patients already being treated with an aldosterone antagonist for a concomitant condition should continue on this.

2.10 Prescribing of isosorbide mononitrate (ISMN)

Wherever possible the use of standard release ISMN should be considered. To prevent the development of nitrate tolerance it is essential that the two doses are prescribed approximately 6–8 hours apart NOT 12-hourly.

The Medicine Clinical Board has approved ward pharmacists using agreed criteria to switch both newly initiated patients and patients on modified release (MR) ISMN on admission from once daily MR ISMN to ISMN bd.

The use of sustained release preparations should be restricted to patients in whom this dosage form is most appropriate.

These patients may include:

- Those already taking a substantial number of medicines or on a complex regimen and in whom a single daily dose would be considered essential to support concordance
- Those who would have difficulty in understanding or complying with doses at 8am and 2pm (times usually suggested)
- Those with nocturnal angina in whom a twice daily dose would be inappropriate
- Heart failure patients receiving nitrates for off loading in whom a twice daily regimen is inappropriate
- Patients on ISMN MR 90mg or 120mg daily
- Patients with unstable angina

Helpful Information

- It is useful to include a comment on the Discharge Advice Letter to Primary Care explaining the reason why a long acting nitrate has been chosen for the individual patient.
- It is important to recognise the place of nitrate therapy in the prophylaxis of angina and ensure that it is in line with evidence-based treatment of ischaemic heart disease. Beta blockers and heart rate control are first line for stable disease.
- Calcium antagonists should be considered as an alternative to a nitrate with the advantage that there is no risk of tolerance developing and 24 hour cover is provided.

2.11 Perhexiline

Perhexiline is initiated by specialists in the management of severe angina pectoris. It is an unlicensed medicine and is not listed in the BNF. Its use MUST be carefully monitored.
All patients started on perhexiline MUST be referred for clinical management/monitoring to the perhexiline clinic run through the cardiology out-patients.

### 2.12 Atrial fibrillation

- Atrial fibrillation may be paroxysmal (self-terminating), persistent (>7 days or requiring cardioversion to restore sinus rhythm) or permanent (electrical cardioversion has failed to restore sinus rhythm).
- Initial assessment should attempt to identify and/or treat any underlying causes (e.g. valvular, ischaemic, hypertensive heart disease, thyrotoxicosis, etc) and any precipitating causes (e.g. alcohol, chest infection, pulmonary embolism, etc).

#### Acute Management (minutes to hours)

Depends on clinical status and duration of AF:

- AF with rapid ventricular rate and haemodynamic compromise (hypotension, chest pain, worsening heart failure). Patient should be anti-coagulated with heparin and assessed by an anaesthetist for emergency electrical cardioversion.
- Well tolerated AF with rapid ventricular rate should be managed initially with heparinisation and rate control. Rate control agents include beta-blockers first line, calcium channel blockers or digoxin (see 'Drugs to control ventricular rate'). In patients with significant structural heart disease, amiodarone may be indicated to control the ventricular rate.

#### Acute Management (hours to days)

Consider restoring sinus rhythm. Method depends on duration of AF, patient symptoms and presence/absence of structural heart disease:

- AF > 24 hours requires 4-6 weeks oral anticoagulation prior to elective cardioversion or in selected cases can be cardioverted sooner if a transoesophageal echocardiogram rules out atrial thrombus.
- AF < 24 hours can be cardioverted electrically or pharmacologically (see 'Drugs to maintain sinus rhythm').

#### Long-term management of atrial fibrillation

The aims of long-term management are to relieve symptoms, prevent thromboembolic complications such as CVA and prevent tachycardia-induced cardiomyopathy resulting in worsening heart failure. One of the following 2 strategies should be employed:

- Maintenance of sinus rhythm using anti-arrhythmic drugs and electrical cardioversion.
- Rate control and anticoagulation.

In patients with atrial fibrillation and other risk factors for stroke (see section "Prevention of Thromboembolism in AF") the long-term decision regarding anticoagulation should be made independently of the long-term strategy of either rhythm or rate control.

#### Drugs to maintain sinus rhythm

These drugs have a direct effect on atrial and ventricular myocardium, are potentially proarrhythmic and should be discussed with a senior colleague before initiation.
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Choice of most appropriate agent (see table) depends on the type of underlying heart disease and potential side-effects.

<table>
<thead>
<tr>
<th>Structural Heart Disease</th>
<th>Reasonable Drug Option</th>
<th>Avoid or extreme caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>All antiarrhythmic agents including Class IC agents e.g. flecainide, propafenone</td>
<td>None</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>Sotalol</td>
<td>All Class IC absolutely contraindicated</td>
</tr>
<tr>
<td></td>
<td>Amiodarone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dronedarone</td>
<td></td>
</tr>
<tr>
<td>Hypertension/Hypertrophy</td>
<td>Class IC</td>
<td>Sotalol</td>
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<td></td>
<td>Amiodarone</td>
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</tr>
<tr>
<td></td>
<td>Dronedarone</td>
<td></td>
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<tr>
<td>Significant Heart Failure</td>
<td>Amiodarone</td>
<td>All Class I agents (see BNF). Sotalol</td>
</tr>
</tbody>
</table>

Drugs to control ventricular rate

These drugs act directly or indirectly on the AV node. They are absolutely contra-indicated in Wolff-Parkinson-White syndrome (pre-excited AF resulting in an irregularly irregular rapid broad complex tachycardia) – specialist advice should be sought. These agents can be administered orally or intravenously in the acute setting and orally for long-term management (see BNF). Adequate rate control often requires combination therapy.

- Beta-blockers. Unless there is a contra-indication a beta-blocker is the drug of first choice.
- Rate-limiting calcium channel blockers. Agents such as verapamil or diltiazem.
- Digoxin. Controls resting ventricular rate by enhanced vagal tone. Does not control ventricular response during exercise. No longer used as a first line agent except in selected patients with heart failure.
  - Loading dose: 1-1.5mg digoxin po in divided doses over 24 hours
  - Maintenance dose: 250 micrograms digoxin od or as per individual requirements

(Note: maintenance dosing at 6pm allows levels to be taken in the morning)

Elderly

- Loading dose: 750 micrograms digoxin in divided doses over 24 hours
- Maintenance dose: 62.5-125 micrograms od

Intravenous digoxin

- Unnecessary for the majority of patients. Where intravenous digitalisation is required give 500 micrograms in 50mL sodium chloride 0.9% or glucose 5% over 2 hours. A further dose of 250-500 micrograms may be given 4 to 8 hours later if necessary. (When switching from intravenous route to oral route may need to increase dose by 20-33% to maintain the same plasma-digoxin concentration e.g. 500 micrograms IV = 625 micrograms po).
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**Digoxin levels**
- Take blood at least 6 hours after an oral dose (4 hours after an IV dose).
  Ref range: 1.0-2.0 micrograms/L

**Prevention of thromboembolism in atrial fibrillation**
- Long term oral anticoagulation (warfarin) should be considered in all high risk patients. The CHA2DS2-VaSC scoring system is useful for identifying patients who would benefit from warfarin therapy:
  - C (congestive heart failure) = 1
  - H (hypertension) = 1
  - A (age > 75 years) = 2
  - D (diabetes mellitus) = 1
  - S (stroke or TIA) = 2
  - V (vascular disease) = 1
  - A (age > 65 years) = 1
  - Sexual category (female) = 1
- Patients with a CHA2DS2-VaSC score ≥ 2 should be offered long term warfarin. Aim for a target INR = 2.5 and an acceptable range between 2.0-3.0.
- Patients with a CHA2DS2-VaSC score = 0 are at low risk and the risk of thromboembolism is similar to the risk of bleeding with an anticoagulant or antiplatelet agent.
- Patients with a CHA2DS2-VaSC = 1 have been shown to do better on warfarin and the pros and cons of anticoagulation should be discussed with these patients. The exception is a female with a CHA2DS2-VaSC = 1. These should be managed as a CHA2DS2-VaSC = 0 (above).

Non-vitamin K antagonist new oral anticoagulants (NOACs)
- Please use link below for guidance on the prescribing of dabigatran, rivaroxaban and apixaban in Cardiff and Vale UHB (or access via Clinical Portal)

Note: Choice of antithrombotic treatment should always be based on balance of benefit and risk in individual patients. These should be reviewed periodically.

Who should be referred to a cardiologist?
- Wolff-Parkinson-White syndrome (pre-excited AF)
- Repeated emergency admissions due to AF
- AF plus medically refractory heart failure
- AF occurring in patients with significant sinus node disease who may benefit from pacemaker implantation
- AF with difficult to control ventricular rates despite appropriate use of AV nodal slowing agents. Selected patients may benefit from a non pharmacological strategy (AV node ablation and pacemaker therapy).

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Cardiovascular System

2.13 Guidance on the safe use of intravenous amiodarone in acute tachycardias and non-pulseless ventricular tachycardia

Intravenous amiodarone should only be prescribed in exceptional circumstances e.g. patients unable to take amiodarone orally and with no hemodynamic instability, pulmonary oedema or myocardial ischaemia.

Never give bolus amiodarone outside the cardiac arrest situation. (Pulseless VT - follow ALS guidelines)

Intravenous amiodarone is contraindicated in patients with significant hemodynamic instability (low blood pressure), radiological or clinical evidence of pulmonary oedema or symptoms of myocardial ischaemia and first line treatment should be electrical cardioversion.

Oral loading with amiodarone is clinically indicated for the majority of patients who require rhythm control and in select patients for rate control if beta blockade is inappropriate.

Preparation and Administration

Please refer to the Injectable Medicines Guide on the Clinical portal for information on the preparation and administration of amiodarone.

2.14 Accelerated hypertension

- Accelerated (malignant) hypertension requires urgent therapy. Nevertheless a precipitate fall in blood pressure is to be avoided. Sublingual nifedipine is no longer indicated. If beta-blockers are not contra-indicated then they are the drugs of choice, together with or followed by a long-acting calcium channel blocker such as nifedipine LA or amlodipine.
- If an intravenous infusion is required then labetalol (combined alpha and beta blockade) is usually appropriate. Remember that labetalol has a much longer half-life than many other cardiovascular drugs used as a continuous infusion and it is easy to overshoot.
2.15 Essential hypertension

NICE CG 127- Hypertension: Clinical management of primary hypertension in adults, August 2011

- Rarely requires urgent treatment. Remember that pain and anxiety can cause high blood pressure, particularly systolic and that the patient should be managed accordingly.

- Establish that hypertension is sustained before stepping in, particularly out of hours. It is rarely necessary to achieve full control quickly.

- Remember to allow time for a drug to exert its full response (e.g. 4 weeks) before increasing the dose or adding something new (unless it is necessary to lower BP more urgently).

- Initiate treatment in people with sustained systolic BP $\geq 180\text{mmHg}$ or diastolic BP $\geq 110\text{mmHg}$ and offer antihypertensive treatment to patients where BP is $\geq 160/100\text{mmHg}$.

- Drug treatment should also be offered to patients with sustained systolic BP between 140mm and 159mmHg or sustained diastolic BP between 90mm and 99 mmHg if target organ damage is present, or there is evidence of established cardiovascular disease or diabetes, or if there is a 10 year cardiovascular disease risk of $\geq 20\%$.

- For patients aged less than 80 years a target clinic BP of lower than $140/90\text{mmHg}$ is recommended. For patients aged over 80 years a target clinic BP of lower than $150/90\text{mmHg}$ is recommended.

- For patients with Type 2 diabetes the BP target is $<140/80\text{mmHg}$ ($<130/80\text{mmHg}$ if there is kidney, eye or cerebrovascular damage) (NICE CG 87, March 2010)

It is important to think about cost effective prescribing in this chronic disease and the lowest price choices in each group are:

- **ACE-inhibitors**: enalapril, lisinopril or ramipril

- **Angiotensin-II receptor antagonists**: losartan is currently the cheapest followed by valsartan capsules (not tablets)

- **Calcium channel blockers**: amlodipine

- **Beta-blockers**: bisoprolol. (generic form is available only in 5 and 10mg dose) – not a preferred initial therapy for hypertension but still indicated in other conditions such as angina, heart failure or after a myocardial infarction. 4th line after other diuretic therapy - except for very specific conditions.

- **Diuretics**: Indapamide 2.5mg od or 1.5mg MR od (not necessary to switch patients already on bendroflumethiazide 2.5mg od) Note- modified release indapamide is more expensive than the standard-release preparation.

Use once daily medication wherever possible.
Cardiovascular System

Choosing drugs for patients newly diagnosed with hypertension

**Abbreviations**

A = ACE inhibitor
ARB = angiotensin-II receptor blocker (low cost)
C = calcium-channel blocker
D = thiazide-type diuretic (indapamide 1.5 mg MR od or 2.5mg od rather than initiating bendroflumethiazide (not necessary to switch existing patients)

### Aged under 55 years

**Step 1**
- A or ARB

**Step 2**
- A or ARB**+ C**

**Step 3**
- A (or ARB) + C + D

### 55 years or older or black patients of any age

**Step 1**
- C *

**Step 2**
- A or ARB**+ C**

**Step 3**
- A (or ARB) + C + D

### Resistant hypertension

A or ARB + C + D + consider diuretic or alpha-or beta-blocker.
(spironolactone 25mg once daily is first choice additional treatment (if the person's blood potassium level is 4.5 mmol/L or less) (unlicensed indication)

* or D as an alternative to C at step 1 or step 2 if C is not tolerated or the person has oedema, evidence of heart failure or a high risk of heart failure

**Offer a low cost ARB in combination with C in black people of African or Caribbean family origin at step 2

### 2.16 Hypertension following a stroke
(see section 2.2)

- Hypertension is common after a CVA. In the early stages cerebral autoregulation is lost and reducing blood pressure can reduce cerebral perfusion, particularly if the reduction is precipitate. Unless the hypertension is very severe (>120mmHg diastolic) then observe initially. Do not use sublingual nifedipine.
2.17 Advanced life support algorithm for the management of cardiac arrest in adults - Resuscitation Council (UK) 2010

Unresponsive?
Not breathing or only occasional gasps

CPR 30:2
Attach defibrillator / monitor
Minimise interruptions

Assess rhythm

Shockable (VF / Pulseless VT)

1 Shock
Immediately resume CPR for 2 min
Minimise interruptions

Non-shockable (PEA / Asystole)

Return of spontaneous circulation
Immediately resume CPR for 2 min
Minimise interruptions

Immediate post cardiac arrest treatment
• Use ABCDE approach
• Controlled oxygenation and ventilation
• 12-lead ECG
• Treat precipitating cause
• Temperature control / therapeutic hypothermia

During CPR
• Ensure high-quality CPR: rate, depth, recoil
• Plan actions before interrupting CPR
• Give oxygen
• Consider advanced airway and capnography
• Continuous chest compressions when advanced airway in place
• Vascular access (intravenous, intraosseous)
• Give adrenaline every 3-5 min
• Correct reversible causes

Reversible causes:
• Hypoxia
• Hypovolaemia
• Hyper-hypokalaemia/metabolic
• Hypothermia
• Thrombosis – coronary or pulmonary
• Tamponade – cardiac
• Toxins
• Tension Pneumothorax
Cardiovascular System

2.18 Tachycardia algorithm (with pulse) – Resuscitation Council (UK) 2010

- Assess using the ABCDE approach
- Give oxygen if appropriate and obtain IV access
- Monitor ECG, BP, \( \text{SpO}_2 \), record 12-lead ECG
- Identify and treat reversible causes (e.g. electrolyte abnormalities)

**Synchronised DC Shock**
- Up to 3 attempts
- **Yes/Unstable**
  - **Adverse features?**
    - Shock
    - Syncope
    - Myocardial ischaemia
    - Heart failure
  - **No/Stable**

**Is QRS narrow (<0.12 sec)?**

- **NARROW**
  - Irregular
    - Seek expert help
  - Regular
    - **Broad QRS**
      - **Is rhythm regular?**
        - **Regular**
        - Possibilities include:
          - AF with bundle branch block
          - Pre-excited AF
          - Polymorphic VT (e.g. torsade de pointes - give magnesium 2g over 10 min)
        - If Ventricular Tachycardia (or uncertain rhythm):
          - Amiodarone 300mg IV over 20-60 min; then 900mg over 24 hours
        - If previously confirmed SVT with bundle branch block:
          - Give adenosine as for regular narrow complex tachycardia
      - If Ventricular Tachycardia (or uncertain rhythm):
        - Amiodarone 300mg IV over 10-20 min and repeat shock; followed by:
        - Amiodarone 900mg over 24 hours

- **BROAD**
  - **Is QRS broad?**
    - **Yes**
      - Seek expert help
    - **No**
      - **NARROW**
        - **Is rhythm regular?**
          - **Regular**
          - Possibilities include:
            - AF with bundle branch block
            - Pre-excited AF
            - Polymorphic VT (e.g. torsade de pointes - give magnesium 2g over 10 min)
          - If Ventricular Tachycardia (or uncertain rhythm):
            - Amiodarone 300mg IV over 10-20 min and repeat shock; followed by:
            - Amiodarone 900mg over 24 hours

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NARROW

Regular

- Use vagal manoeuvres
- Adenosine 6mg rapid IV bolus; if unsuccessful give 12 mg; if unsuccessful give further 12mg.
- Monitor ECG continuously

Irregular

Narrow QRS
Is rhythm regular?

Sinus rhythm restored?
Yes

Probable re-entry paroxysmal SVT:
- Record 12-lead ECG in sinus rhythm
- If recurs, give adenosine again & consider choice of anti-arrhythmic prophylaxis

No

Seek expert help

Irregular Narrow Complex Tachycardia

Probable AF
Control rate with
- Beta-Blocker or diltiazem
- Consider digoxin or amiodarone if evidence of heart failure

Possible atrial flutter
- Control rate (e.g. beta-blocker)
2.19 Bradycardia algorithm - Resuscitation Council (UK) 2010

- Assess using the ABCDE approach
- Give oxygen if appropriate and obtain IV access
- Monitor ECG, BP, SpO₂, record 12-lead ECG
- Identify and treat reversible causes (e.g. electrolyte abnormalities)

**Adverse features?**
- Shock
- Syncope
- Myocardial ischaemia
- Heart failure

**Atropine**
500 micrograms IV

**Satisfactory response?**

* **Interim measures:**
  - Atropine 500 micrograms IV repeat to maximum of 3mg
  - Isoprenaline 5 micrograms min⁻¹ IV
  - Adrenaline 2-10 micrograms min⁻¹ IV
  - Alternative drugs *
  OR
  - Transcutaneous pacing

* **Risk of asystole?**
  - Recent asystole
  - Möbius II AV block
  - Complete heart block with broad QRS
  - Ventricular pause >3s

* **Alternatives include:**
  - Aminophylline
  - Dopamine
  - Glucagon (if beta-blocker or calcium-channel blocker overdose)
  - Glycopyrrolate can be used instead of atropine
2.20 Prevention of Cardiovascular Disease (CVD)


- Target people at high risk (CVD risk of ≥20% over 10 years) of developing symptomatic atherosclerotic disease. This will include:
  i. People with any form of established atherosclerotic CVD
  ii. People with diabetes mellitus (Type 1 or 2)
  iii. Asymptomatic individuals without established CVD with a CVD risk of ≥20% over 10 years.

- In addition, other people with particularly elevated single risk factors also require CVD prevention because they too are at high CVD risk, regardless of the presence of other risk factors:
  i. elevated BP ≥160mmHg systolic or ≥100mmHg diastolic, or lesser degrees of BP pressure elevation with target organ damage.
  ii. elevated total cholesterol to high density lipoprotein (HDL) cholesterol ratio ≥6.0
  iii. familial dyslipidaemia, such as familial hypercholesterolaemia or familial combined hyperlipidaemia.

People with a family history of premature CVD should be assessed for their cardiovascular risk and then managed appropriately.

- Maintain BP <140/85mmHg
- Statins are recommended for all high risk people with established atherosclerotic disease, and in most people with diabetes, and others at high total risk of developing CVD.
- Aspirin 75mg daily is recommended for life for all people with coronary or peripheral atherosclerotic disease. If aspirin is not tolerated (either proven hypersensitivity to aspirin or a history of severe dyspepsia induced by low dose aspirin despite treatment with a proton pump inhibitor), then clopidogrel 75mg daily is appropriate.
- On current evidence, aspirin is no longer recommended for primary prevention of cardiovascular disease.

Primary prevention of cardiovascular disease (CVD)

NICE CG67 - Lipid modification, May 2008

- Assess modifiable risk factors-smoking status, alcohol consumption, blood pressure, BMI, fasting total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides, fasting blood glucose, renal function, liver function (transaminases), thyroid-stimulating hormone (TSH) if dyslipidaemia is present.
- The estimated CVD risk should be increased by a factor of 1.5 in people with a first-degree relative with a history of premature CHD (age at onset younger
Cardiovascular System

than 55 in fathers, sons or brothers or younger than 65 in mothers, daughters or sisters).
• The estimated CVD risk for men with a South Asian background should be increased by a factor of 1.4
• CVD risk may be underestimated in people who are already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking.
• Statin therapy is recommended as part of the management strategy for adults ≥ 40 years who have cardiovascular disease risk of ≥ 20% over 10 years. For patients less than 40 years old consider simvastatin where the cardiovascular risk factor profile appears particularly poor (multiple features of the metabolic syndrome, presence of conventional risk factors, microalbuminuria, at risk ethnic group or strong family history of premature cardiovascular disease).
• Initiate simvastatin 40mg* nocte. (If there are potential drug interactions, or simvastatin is contraindicated, a lower dose or alternative preparation such as pravastatin may be chosen.
• Higher intensity statins should not routinely be offered to people for the primary prevention of CVD**.
• A target for total or LDL-cholesterol is not recommended for people who are treated with a statin for primary prevention of CVD.
• Once a person has been started on a statin for primary prevention repeat lipid measurement is unnecessary. Clinical judgement and patient preference should guide the review of drug therapy and whether to review the lipid profile.
• Ezetimibe monotherapy is ONLY recommended as an option in people who are intolerant to statin therapy or where there are contraindications to statin therapy.
• Ezetimibe may be used in combination with a statin in patients with familial hypercholesterolemia (intensify the statin first) if serum total or LDL-cholesterol is not adequately controlled (NICE TA 132).
• Fibrates, nicotinic acid or anion exchange resins as monotherapy or in combination with a statin are not recommended for the primary prevention of CVD.
• The combination of a fish oil supplement with a statin should not be offered for the primary prevention of CVD.

Secondary prevention of CVD
NICE CG 67- Lipid modification, May 2008
• Assess modifiable risk factors (as for primary prevention)
• Initiate simvastatin 40mg* nocte. Change to a more potent statin if a total cholesterol of less than 4mmol/L or an LDL-cholesterol of less than 2mmol/L is not attained.
• Patients with acute coronary syndrome should be treated with a higher intensity statin (i.e. statins used in doses that produce greater cholesterol reduction).*note maximum dose of simvastatin is 20mg daily with concomitant amiodarone, verapamil, diltiazem or amlopine and 10mg daily with concomitant fibrates (except fenofibrate)
**In general simvastatin 40mg nocte will result in a significant decrease in LDL-cholesterol but inter-patient response does vary. It is important that clinical discretion is exercised in individual cases with regard to dosage and choice of statin used (local expert opinion)
lowering than simvastatin 40mg daily). A fasting lipid sample should be taken about 3 months after the start of treatment. Current practice is to swap to a more potent statin rather than increasing to simvastatin 80mg daily due to the increased side effect profile.

- An ‘audit’ level of total cholesterol of 5mmol/L should be used, in recognition that more than half of patients will not achieve a total cholesterol of less than 4mmol/L and LDL-cholesterol of less than 2mmol/L.
- Ezetimibe (see previous section) - consider intensifying lipid management therapy with a more effective statin (than simvastatin 40mg) or ezetimibe in diabetic patients with existing or newly diagnosed CVD or those with an increased albumin excretion rate to achieve a serum total cholesterol of less than 4mmol/L or LDL less than 2mmol/L (NICE CG87). Treatment intensification with a more potent statin would be the preferred Cardiff and Vale UHB strategy for patients not at LDL targets.
- If high cardiovascular risk and triglyceride levels remain in the range 2.3-4.5 mmol/L, despite statin therapy, consider adding a fibrate.

Consider referral of patients with mixed dyslipidaemia of Type 2 diabetes to a specialist lipid clinic if triglycerides remain persistently elevated and particularly so when accompanied by a lowered HDL-cholesterol.

### 2.21 Statin Monitoring

*NICE CG67- Lipid modification, May 2008*

- Baseline liver enzymes should be measured before starting a statin. Liver function (transaminases) should be measured within 3 months of starting treatment and at 12 months but not again unless clinically indicated.
- People who have liver enzymes (transaminases) that are raised but are less than 3 times the upper limit of normal should not be routinely excluded from statin therapy.
- If a person taking a statin starts taking additional drugs, or needs treatment for a concomitant illness that interferes with metabolic pathways or increases the propensity for drug and food interactions, consider reducing the dose of the statin, changing to one that does not interact or temporarily or permanently stopping it.
- People treated with a statin should be advised to seek medical advice if they develop muscle symptoms (pain, tenderness or weakness). If this occurs, plasma creatine kinase should be measured.
- Creatine kinase should not be routinely monitored in asymptomatic people who are being treated with a statin.
- Discontinue statin if a person develops unexplained peripheral neuropathy and seek specialist advice.
2.22 Peripheral arterial vascular disease

NICE TA 223 - Cilostazol, naftidrofuryl oxalate, pentoxifylline and inositol nicotinate for the treatment of intermittent claudication in people with peripheral arterial disease, May 2011

- Modification of risk factors, e.g. offer advice on smoking cessation, exercise and weight loss, lower cholesterol, treat hypertension and control glycaemia in patients with diabetes.

- Routine combination of aspirin with clopidogrel in patients with peripheral arterial vascular disease has not yet been established. Please seek advice of a senior colleague before prescribing.

- In patients with either intermittent claudication or rest pain, clopidogrel 75mg daily is recommended instead of aspirin 75mg daily.

- Clopidogrel 75mg daily is recommended instead of aspirin 75mg daily following either bypass grafting or balloon angioplasty.

- Naftidrofuryl oxalate (100-200mg three times a day) is an option for the treatment of intermittent claudication in people with peripheral arterial disease. Cilostazol, pentoxifylline and inositol nicotinate are not recommended.

2.23 Iloprost

(unlicensed)

Please consult with a senior medical colleague regarding the initiation of iloprost and duration of therapy.

Indications

Buerger’s disease, treatment of patients with severe peripheral arterial occlusive disease (particularly those at risk of amputation and in whom surgery or angioplasty is not possible) and treatment of patients with severe disabling Raynaud’s phenomenon unresponsive to other therapies.

Common side effects associated with iloprost include facial flushing, headache, nausea and vomiting, and abdominal cramps.
Administration of iloprost via syringe driver

Dilute 0.5mL (50 micrograms) ampoule of iloprost with 25mL sodium chloride 0.9% or glucose 5%.

Dose titration:

Day 1

Start the infusion at 1mL/hour. Check the patient’s pulse and blood pressure after 30 minutes.

If this dose has been tolerated, increase to 2mL/hour for 30 minutes. Check the patient’s pulse and blood pressure.

If unacceptable side-effects have occurred, decrease to 1mL/hour.

If this dose has been tolerated, increase to 3mL/hour for 30 minutes. Check the patient’s pulse and blood pressure.

If unacceptable side-effects have occurred, decrease to 2mL/hour.

If this dose has been tolerated, increase to 4mL/hour for 30 minutes. Check the patient’s pulse and blood pressure.

If unacceptable side-effects have occurred, decrease to 3mL/hour.

Check the patient’s pulse and blood pressure every 30 minutes.

Continue until the optimal rate is established. For the majority of patients the rate will not exceed 5mL/hour.

After 6 hours, stop the infusion.

Day 2 and 3

Follow the procedure given for Day 1, to confirm the optimal dosage.

Day 4 to the end of treatment

Start the infusion at the optimal rate and maintain the infusion for 6 hours.

* For patients who weigh less than 75kg, the optimal rate seldom exceeds 4mL/hour

NB If at any time the patient experiences unacceptable side-effects, the infusion rate should be reduced by 1mL/hour. Side-effects will then rapidly resolve.

NB If the following symptoms occur:

• a persistent, clinically significant drop in blood pressure
• persistent, clinically significant tachycardia
• vagal reaction with bradycardia, nausea and vomiting

the infusion should be stopped until the situation returns to normal. Wait for one hour and then recommence at half the previous flow rate.

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2.24 Deep vein thrombosis

2.24.1 Deep Vein Thrombosis (DVT) Service

The Cardiff and Vale UHB DVT Service is run by Venous Thrombosis Nurse Specialists with clinical support from the Haematology department. It is based in Doppler Ultrasound, Medical Physics department, Ground Floor B Block, UHW.

- **Hours of Operation** - Monday to Friday (except Bank Holidays) 08:30 – 16:30

- **Out of Hours** - Refer to on-call medical team. The DVT clinic will assume management of these referrals (if appropriate) from MAU on the next working day.

- To complete all relevant investigations the patient must arrive by 15:00hrs.

- To refer please call: Ext 48729 or Bleep Nurse Specialist on 6492 via switchboard.

The following details will be required:

- Your name and telephone number
- Patient’s name and address
- Patient’s date of birth
- Patient’s telephone number
- Reason for referral

Please ensure the patient attends with a referral letter including a list of current medication **(or fax to 02920 74477)**. If transport is required this must be arranged by the patient’s GP, please note that the DVT clinic cannot accept patients on stretchers or trolleys. Such patients will need to be discussed with Doppler ultrasound directly on Ext 43547.

**Patients must be:**

- 18yrs or over
- Registered with a Cardiff and Vale GP
- Suitable for ambulatory care
- Patients must be medically stable with no concurrent acute illnesses which may require admission
- Patients must be concordant with treatment

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**Exclusion Criteria** (refer directly to on-call medical team)

- < 18yrs of age
- Suspicion of pulmonary embolism
- Suspicion of cardiac chest pain
- Underlying medical conditions requiring admission
- Gastro-intestinal, genitourinary or inter-cranial bleed within last 4 weeks
- Known liver disease
- Renal insufficiency (creatinine > 200 micromol/L)
- Inherited bleeding disorder
- Thrombocytopenia (platelet count < 100 x 10^9/L)

### 2.24.2 Diagnostic algorithm for suspected DVT

**Pre-test probability assessment**

An initial Wells Score will be used to risk stratify the patient as *likely* or *unlikely* to have a DVT in accordance with the **NICE CG144, June 2012 “Venous thromboembolic diseases: the management of venous thromboembolic diseases”**.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer (treatment ongoing, treatment within 6 months, or palliative)</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis or recent plaster immobilisation of the lower extremities</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden for &gt; 3 days or more major surgery &lt; 12 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Localised tenderness along the distribution of the deep venous system</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swollen</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling &gt;3cm compared to the asymptomatic side (measure 10cm below tibial tuberosity)</td>
<td>1</td>
</tr>
<tr>
<td>Pitting oedema confined to the symptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Dilated (non-varicose) superficial veins in symptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis* (as likely or more than that of DVT) – See below</td>
<td>-2</td>
</tr>
</tbody>
</table>

**DVT likely** 2 points or more  
**DVT unlikely** 1 point or less

*Alternative diagnoses to consider*

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis</td>
<td>Torn gastrocnemius (calf) muscle</td>
</tr>
<tr>
<td>Baker’s cyst</td>
<td>Acute arterial ischaemia</td>
</tr>
<tr>
<td>Haematoma</td>
<td>Compartment syndrome</td>
</tr>
<tr>
<td>Fracture</td>
<td>Superficial thrombophlebitis</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Post thrombotic syndrome</td>
</tr>
<tr>
<td>Lymphoedema</td>
<td>Hypoproteinaemia (e.g. cirrhosis, nephrotic syndrome)</td>
</tr>
</tbody>
</table>

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Cardiovascular System

D-Dimer
A D-dimer will be measured in those patients with an “unlikely” Well’s score. However a D-dimer cannot be used as part of the diagnostic algorithm in patients who have already received a dose of low molecular weight heparin (risk of false negative results) and therefore these patients will undergo Doppler ultrasound irrespective of their Well’s score.

Ultrasound
In accordance with NICE CG144 patients, whose ultrasound scan will be delayed by >4hrs, will need to be given a treatment dose of LMWH (Out of Hours patients). Patients referred to the DVT service will undergo a full leg Doppler ultrasound performed in the Medical Physics dept at UHW.

N.B. Patients imaged at UHL only receive proximal (above knee) scans therefore those who have a negative Doppler but have had ‘Likely’ Wells Score and a positive D-Dimer will require a repeat ultrasound in a week (as per NICE CG144). Alternatively these patients can be referred to the DVT Service at UHW for full leg imaging.

DVT not identified
Patients will be discharged from the DVT service and the result will be sent to the referring doctor.

DVT Confirmed
These patients will be managed by the DVT service (Ext 48729 or Bleep DVT Nurse on 6492 via switchboard)

2.24.3 Out patient treatment of DVT
Will comprise one of the following:

1. LMWH (minimum 5 days) + warfarin
   - Enoxaparin 1.5mg/kg SC daily until INR > 2 for 2 consecutive days.
   - NB: eGFR < 30mL - enoxaparin 1mg/kg SC daily (discuss with haematology SpR – anti-Xa monitoring).
• Warfarin will be initiated as per the All Wales loading schedule. However elderly / underweight patients will receive lower loading doses.

2. LMWH as an alternative to warfarin (please contact haematology SpR bleep 5886)
• All pregnant patients (enoxaparin 1mg/kg SC twice daily – use booking weight)
• Patients with an underlying malignancy will be considered for continuing LMWH for 6 months rather than warfarin. This carries a similar risk of bleeding but halves recurrences.

3. Rivaroxaban as an alternative to warfarin (please contact haematology SpR bleep 5886)

2.24.4 Duration of anticoagulation

<table>
<thead>
<tr>
<th>Indication</th>
<th>Duration</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st idiopathic proximal DVT</td>
<td>≥ 3 months</td>
<td>Thrombosis Clinic</td>
</tr>
<tr>
<td>1st precipitated proximal DVT</td>
<td>3 months</td>
<td>*No follow up</td>
</tr>
<tr>
<td>1st idiopathic distal DVT</td>
<td>3 months</td>
<td>*No follow up</td>
</tr>
<tr>
<td>1st precipitated distal DVT</td>
<td>3 months</td>
<td>*No follow up</td>
</tr>
<tr>
<td>Recurrent DVT not on warfarin / sub-therapeutic INR</td>
<td>≥ 3 months</td>
<td>Thrombosis Clinic</td>
</tr>
<tr>
<td>Recurrent DVT on warfarin and therapeutic INR</td>
<td></td>
<td>Thrombosis Clinic</td>
</tr>
<tr>
<td>DVT in patient with active cancer</td>
<td>6 months</td>
<td>Thrombosis Clinic</td>
</tr>
<tr>
<td>Upper limb DVT</td>
<td>3 months</td>
<td>Thrombosis Clinic</td>
</tr>
</tbody>
</table>

*Patients with a family history of DVT / PE will be followed up in Thrombosis Clinic

If the patient is on anti-platelet medication a doctor should review whether this is to continue, whilst the patient is on anticoagulation

Long-term treatment will be considered for
• recurrent thromboses
• patients with on-going risk factors such as cancer
• a first unprovoked proximal DVT (or PE). The ACCP and BCSH guidelines recommend long-term treatment for unprovoked VTE where there is a low risk of bleeding and where anticoagulant control is good.

This may be felt to be particularly the case:
  o if D-dimers are raised one month after discontinuing anticoagulation
  o presence of antiphospholipid antibodies
  o in a male
  o in those with PTS (post-thrombotic syndrome)

2.24.5 Compression stockings
• All patients with symptomatic proximal DVT (and those with severe symptoms with a distal DVT) will be assessed for below knee compression hosiery and prescribed if there are no contraindications (see below).
European class 2 (25-32mmHg) below knee compression stockings are prescribed.

- Patients should be advised to wear the stocking during the day for two years.
- The patient should be re-measured for new stockings every six months.

Contra-indications are:

- Known / suspected peripheral arterial disease or peripheral neuropathy – do not use hosiery if suspected until investigations completed.
- Leg oedema or pulmonary oedema from congestive cardiac failure (CCF).
- Slow capillary filling – (pinched nail bed or pad of toe that takes more than 3 seconds to return to normal colour).
- History of intermittent claudication or rest pain.
- Known allergies to the components/materials of the stockings.
- Diabetes – if there is known / suspected peripheral arterial disease or peripheral neuropathy.
- Fragile ‘tissue paper’ skin.
- Absent/weak foot pulses.
- Cellulitis and/or leg/foot ulceration.
- Pressure ulcers to heels or any area of foot or lower leg.
- Trophic skin changes (cold, pale, shiny, hairless leg).

Hosiery will be prescribed by ART nurses days 5-10, but if acute swelling has not settled the patient can be brought back after 2-3 weeks.

2.24.6 Suspected upper limb DVT

- These patients will all have a Doppler ultrasound examination
- Patients will be considered for anticoagulation or thrombolysis
- ALL patients should be discussed with a vascular surgeon re: thrombolysis
  - CXR requesting “thoracic outlet views” and C-spine to look for cervical rib(s)
  - Doppler assessment for thoracic outlet compression
- Recurrence rates for upper limb DVT after anticoagulant treatment for three months are very low and it is likely that prolonged anticoagulation is not required for the majority of patients.
- For most patients with upper limb DVT in association with an indwelling central or peripheral venous catheter, the catheter should not be removed if it is functional and there is an ongoing need for the catheter. If the catheter is removed anticoagulant treatment should not be shortened to less than 3 months.
- Elastic compression is not used routinely but may be considered for patients who have persistent upper limb oedema and pain.

For advice on initiating anticoagulation and the indicated duration, see section 2.26.
2.24.7 Anti-Xa monitoring
- LMWH accumulates in patients with renal failure (eGFR <30mL/min)
- Either change to unfractionated heparin or monitor Anti-Xa levels
- A blood sample (blue citrate bottle) must be taken 4 hours after the last dose of enoxaparin for Anti-Xa monitoring and should be discussed with the haematology laboratory in advance
- The need for Anti-Xa monitoring and interpretation of results should be discussed with a haematologist (coagulation SpR / consultant)

2.25 Pulmonary embolism

A NEW PE PATHWAY is under development – contact Dr Simon Barry

2.26 Oral anticoagulation - initiation of warfarin
- All prescribers must ensure their personal competency in prescribing and monitoring warfarin having completed relevant training. Suitable training materials have been developed by the NPSA and are available through BMJ learning http://learning.bmj.com
- In the absence of a contraindication, commence warfarin when diagnosis confirmed.
- Patients with cancer-associated VTE should initially be treated for 6 months with a therapeutic dose of LWMH rather than warfarin.
- Obtain a baseline coagulation screen and INR.
- Prescribe warfarin at 2pm on the regular side of the drug chart.
- Complete an Adult In-patient Warfarin Treatment Chart with the patient’s details, indication and target INR.
- Complete the Warfarin Care Pathway (attached to the Adult Inpatient Warfarin Treatment Chart). Complete section 1 for all newly initiated patients and section 2 for all patients discharged on warfarin. The patient should also sign all relevant sections.
- If the pre-treatment INR is <1.4 then the nomogram on the Adult Inpatient Warfarin Treatment Chart may be used to achieve a target INR of 2.5. N.B. Nomogram is not suitable for other target INR e.g. valve replacement.
- Measure the INR daily for the first 4 days and adjust dose as per nomogram. If LWMH is required then it should be continued for at least 5 days and until the INR is greater than or equal to 2 for at least 24 hours.

Irrespective of whether the nomogram is used, all patients should have a documented INR within the first 24 hours.
- Do not use the nomogram for patients already on warfarin (induction only).
- Caution in elderly patients or those patients with heart failure, liver disease, changing drug therapy or those immediately post-op since their sensitivity to warfarin may vary with time.
Cardiovascular System

- Many drug-drug interactions occur with warfarin. Always check patient’s concomitant medication.
- Ensure patient has an Oral Anticoagulant Therapy information folder (containing patient information booklet, record sheet, record book and alert card)

For patients who do not require heparin, a slow loading schedule for warfarin should be considered.

**Warfarin slow loading schedule**

Ensure INR <1.4 before treatment. If INR >1.4 consider reasons for raised INR and consider if warfarin definitely indicated.

Starting dose: warfarin 3mg oral daily at 6 pm

Check INR at day 8

<table>
<thead>
<tr>
<th>INR</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.4</td>
<td>Increase to 6mg and check in 1 week (see below for day 15)</td>
</tr>
<tr>
<td>1.4 – 1.5</td>
<td>Increase to 5mg and check in 1 week</td>
</tr>
<tr>
<td>1.6 – 1.8</td>
<td>Increase to 4mg and check in 1 week</td>
</tr>
<tr>
<td>1.9 – 2.1</td>
<td>Maintain 3mg, check in 1 week</td>
</tr>
<tr>
<td>2.2 – 2.5</td>
<td>Reduce to 2.5mg, check in 1 week</td>
</tr>
<tr>
<td>2.6 – 2.7</td>
<td>Reduce to 2mg, check in 1 week</td>
</tr>
<tr>
<td>2.8 – 3.0</td>
<td>Omit 1-2 days, reduce to 1mg and check in 1 week</td>
</tr>
<tr>
<td>&gt;3.0</td>
<td>Stop, check in 3-5 days. Restart at 1mg if settled and warfarin definitely indicated</td>
</tr>
</tbody>
</table>

Day 15

(if the patient has received 6mg during the second week because of inadequate response to 3mg)

<table>
<thead>
<tr>
<th>INR</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.4</td>
<td>Increase to 10 mg and check in 1 week</td>
</tr>
<tr>
<td>1.4 – 1.6</td>
<td>Increase to 8 mg and check in 1 week</td>
</tr>
<tr>
<td>1.7 – 1.8</td>
<td>Increase to 7mg and check in 1 week</td>
</tr>
<tr>
<td>1.9 – 2.4</td>
<td>Maintain 6mg, check in 1 week</td>
</tr>
<tr>
<td>2.5 – 2.9</td>
<td>Reduce to 5mg and check in 1 week</td>
</tr>
<tr>
<td>3.0 – 4.0</td>
<td>Consider omitting 1-2 days and reduce to 4mg, check in 1 week</td>
</tr>
<tr>
<td>4.1 – 5.0</td>
<td>Omit 2 days, and reduce dose by 1-2mg</td>
</tr>
<tr>
<td>&gt;5.0</td>
<td>Omit 3 days and recheck INR</td>
</tr>
</tbody>
</table>

Janes et al. Safe introduction of warfarin for thrombotic prophylaxis in atrial fibrillation requiring only a weekly INR. Clinical and Laboratory Haematology 2004; 26: 43-47

2.27 Maintenance of warfarin started prior to admission

- On admission, check INR, patient’s usual dose and factors that may have affected the results (e.g. missed doses) before prescribing next dose. Review also the clinical indication for warfarin and if continued therapy is indicated in view of patient’s admission.
Before prescribing for an existing patient taking warfarin ensure that appropriate monitoring is being undertaken - ask to see the patient's monitoring booklet (outpatients or new admissions) or Adult Inpatient Warfarin Treatment Chart.

Follow advice on maintenance dosing on Adult Inpatient Warfarin Treatment Chart. (see below)

### MAINTENANCE dosing for all patients

<table>
<thead>
<tr>
<th>Target INR</th>
<th>Actual INR</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>1.8 – 3.2</td>
<td>DO NOT ADJUST DOSE</td>
</tr>
<tr>
<td>3.5</td>
<td>2.8 – 4.2</td>
<td>MONITOR INR EVERY 3-4 DAYS</td>
</tr>
</tbody>
</table>

- If the patient's INR lies within the target range, continue with his/her usual dose of warfarin.
- If the INR is <1.5 use a therapeutic dose of low molecular weight heparin until the INR is in the target range for 2 consecutive days.
- If small dosage adjustments of warfarin are required, increase or decrease the dose by approximately 25% and monitor the INR daily to determine the trend.
  - Do not alter the dose more frequently than every 3-4 days.
- If the INR becomes unstable when the patient is acutely unwell, consider cessation of warfarin and switching to a therapeutic dose of low molecular weight heparin.
- **If you are initiating or stopping a medicine that may interact with warfarin (e.g. antibiotics) be aware that it may de-stabilise the INR approximately three days later.**

When adjusting maintenance doses of warfarin consider the percentage change in dose e.g. 1mg increase will not have the same effect for patients on 1mg daily as patients on 10mg daily. Following a dose change, allow at least 3 days to stabilise before further change.

#### 2.28 Warfarin – perioperative management

Refer to the guidelines for the prescription and administration of bridging therapy for adult patients receiving warfarin therapy undergoing elective surgical procedures available on the clinical portal for more information.

#### 2.29 Warfarin – discharge

- If the patient was admitted on warfarin check their usual INR monitoring arrangements.

Ensure all clinical staff are aware of the options available for INR monitoring of patients that are fit for discharge:
- Patient's general practitioner
- INR clinic at UHW (twice weekly monitoring service)
- INR clinic at UHL (once a week monitoring service)
Cardiovascular System

- Newly diagnosed DVT (Acute Response Team)

The patient’s INR monitoring must be confirmed by one of these services prior to discharge from hospital (section 2 Warfarin Care Pathway)

If a patient cannot be seen by one of these services, the patient’s INR monitoring **MUST** remain the responsibility of the hospital consultant until safe INR monitoring arrangements are made for the patient.

- Ensure that the patient’s anticoagulant record is completed and the patient is provided with dosing advice until their next INR measurement.
- Ensure that the patient has an appointment booked with monitoring service before discharge (or if after discharge, the patient must be contacted).
- Complete section two of Warfarin Care Pathway for all patients discharged on warfarin.

Top copies of both the care pathway and the Adult Inpatient Warfarin Treatment Chart should be given to the patient/carer for presentation before or at the first monitoring appointment. If the patient is for follow up in the UHB Anticoagulant clinics the copies can be attached to the referral clinical management plan and sent directly to the clinic.

### 2.30 UHB anticoagulant clinics

A Haematology anticoagulant clinic is run by pharmacists on Monday and Thursday afternoon in Clinic 6, UHW. Contact the INR pharmacist on bleep 07623 905674 in order to refer a patient. A referral form must be completed before the patient is seen. (See link below or access via Clinical Portal)

http://www.cardiffandvale.wales.nhs.uk/pls/portal/docs/PAGE/CARDIFF_AND_VALE_INTRANET/TRUST_SERVICES_INDEX/PHARMACY_CP/OUTPATIENTS_REFERALS/INR%20CLINIC%20REFERRAL%20220212.PPT

The anticoagulation clinic provides an INR monitoring service. The decision to initiate/continue anticoagulation is a medical decision and remains the responsibility of the referring clinician. An anticoagulation clinic is run weekly on a Wednesday as part of the general haematology clinic at UHL.
2.31 Guidelines for the management of excessive oral anticoagulation

1) Patients with prosthetic heart valves should be managed by the department of Cardiothoracic Surgery. Contact the cardiothoracic surgical SpR on-call who will discuss the details with the appropriate consultant, if necessary.
2) For all other patients the following recommendations are adapted from those of the British Society for Haematology. If you are unsure, consult a haematologist (or cardiac surgeon if the patient has a heart valve).

INR > 5.0 – no bleeding
• Omit one to two doses of warfarin
• Reduce the dose following the “Maintenance of warfarin” table on Adult Inpatient Warfarin Treatment Chart
• Investigate cause of elevated INR
• Restart when INR <5.0
• Assess patient for their risk of bleeding: recent surgery/trauma, extensive bruising, minor mucosal bleeding.
  If at high risk of bleeding give vitamin K 2mg orally:
  Use 0.2mL Konakion MM paediatric (phytomenadione 2mg in 0.2mL). Draw up using oral dispenser provided and then drop onto the tongue.
• Recheck INR after 24 hours, repeat dose of vitamin K if INR is still too high.

INR > 8.0 – no bleeding
Should receive 1-5mg of oral vitamin K

Non-major bleeding
Anticoagulation reversal for non-major bleeding should be with 1-3 mg intravenous vitamin K

Major bleeding: Life or limb threatening bleeding, including intracranial haemorrhage
• Stop warfarin
• Give 5mg vitamin K IV (0.5mL phytomenadione 10mg/mL – Konakion MM.)
  Give as an IV bolus over 3-5 minutes undiluted or diluted with 10-20mL of glucose 5% to aid slow administration.
• Give prothrombin complex concentrate (PCC - Factor II, VII, IX and X concentrate) – dose to be advised by haematologist. Dissolve in water for injection as per manufacturer’s guidance, using an aseptic technique and the provided transfer device. Administer over 10 minutes. See local protocol for further details on administration.
• Repeat INR within 1 hour of giving of PCC – consider further dose if INR remains >1.5 and patient still bleeding (discuss with haematologist).
• Consider risk-benefit of recommencing warfarin.

Notes
Fresh frozen plasma should not be used to reverse warfarin unless specifically recommended by haematology. This is because it has poor efficacy compared to prothrombin complex concentrates and there is a potential risk of transfusion

The online Good Prescribing Guide is updated as new guidance becomes available and agreed and therefore may contain more up to date information than the printed copy. The online Guide is available via the intranet or via www.wmct.nhs.uk.
Cardiovascular System

reactions and transmission of vCJD.

Logistics
Prothrombin complex concentrate (Octaplex) is kept in blood bank at UHW and UHL and is used only under the direction of a haematologist. Administration should be by a doctor of the team looking after the patient under guidance of a haematologist.

2.32 Variable rate intravenous unfractionated heparin (IV UFH)

**NB:** Prescribe on the patient’s in-patient medication chart (write “heparin continuous infusion-see heparin chart”) and on the separate IV UFH chart

- Check baseline coagulation screen (PT, APTT and fibrinogen)
- Use **ready diluted** heparin 20,000 units in 20mL ampoules.
- **Heparin induced thrombocytopenia** (HIT). Check FBC at baseline and on alternate days. Contact haematology **urgently** if platelet count falls >30% of pre-heparin baseline or thrombosis occurs whilst on treatment. Risk highest between day 5 and 14 of treatment.
- Do not use in severe liver impairment. Use with caution in renal failure.
UNFRACTIONATED HEPARIN INTRAVENOUS INFUSION PROTOCOL

Prescribe heparin infusion on the patient’s in-patients medication chart, as follows:

Commencing unfractionated heparin (obtain directly from pharmacy)
Prescribe initial bolus of heparin followed by infusion rate as directed below:

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Heparin bolus dose (units over 5 minutes)</th>
<th>Infusion rate Units/hour</th>
<th>Tick dose</th>
<th>Doctor’s signature</th>
<th>Bleep</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 67</td>
<td>4,000</td>
<td>800</td>
<td>0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 67</td>
<td>5,000</td>
<td>1000</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Monitoring unfractionated heparin

Target APTT Ratio Range: 1.5 - 2.5
Check APTT ratio 6 hours after starting the infusion. Adjust dose according to the APTT ratio as follows:

<table>
<thead>
<tr>
<th>APTT ratio</th>
<th>Change to Heparin infusion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 6</td>
<td>Discontinue infusion temporarily (30-60 min) and contact haematology SpR for advice</td>
</tr>
<tr>
<td>5.1 – 6.0</td>
<td>Reduce infusion by 500 units (0.5 mL) per hour</td>
</tr>
<tr>
<td>4.1 – 5.0</td>
<td>Reduce infusion by 300 units (0.3 mL) per hour</td>
</tr>
<tr>
<td>2.6 – 4.0</td>
<td>Reduce infusion by 100 units (0.1 mL) per hour</td>
</tr>
<tr>
<td>1.5 – 2.5</td>
<td>No Change</td>
</tr>
<tr>
<td>1.2 – 1.4</td>
<td>Increase infusion by 200 units (0.2 mL) per hour</td>
</tr>
<tr>
<td>&lt; 1.2</td>
<td>Increase infusion by 400 units (0.4 mL) per hour</td>
</tr>
</tbody>
</table>

• If a dose adjustment is made check the APTT ratio between 4-6 hours after the change is implemented
• Continue to adjust as per protocol until APTT ratio is in target range.
• Once in target range check APTT ratio at least daily, or if clinical situation changes.
• Monitor closely for signs of bleeding – BP, pulse, haemoglobin and clinical signs.
• Review requirement for unfractionated heparin daily; consider use of alternative anticoagulant where possible.

2.33 Reversal of low molecular weight and unfractionated heparin

If reversal of low molecular weight or unfractionated heparin required please seek advice from a haematologist (coagulation SpR / consultant).
2.34 Heparin-Induced Thrombocytopenia (HIT)

DEFINITION

**Non surgical patients:** a fall in the platelet count of \(\geq 50\%\) from that recorded immediately before commencing heparin therapy, occurring \(\geq 5\) days (and usually <10 days) after initial heparin exposure.

**Surgical patients:** a fall in the platelet count of \(\geq 50\%\) from the first post-operative platelet counts, occurring \(\geq 5\) days (and usually <10 days) after initial heparin exposure.

NOTES

- In surgical patients a fall in platelets by \(\geq 50\%\) from peak post-operative count may not result in thrombocytopenia. A high index of suspicion is needed.
- Patients with prior heparin exposure within the previous 100 days may develop thrombocytopenia <5 days.
- Severe thrombocytopenia (<15 \(\times\) 10\(^9\)/L) is unusual.
- HIT may rarely occur with low molecular weight heparin (LMWH) but significant cross-reactivity may occur and LMWHs are contraindicated in confirmed and suspected cases of HIT.
- Patients with HIT tend not to bleed.
- Untreated, HIT is associated with thrombosis in up to 50% of cases. Thrombosis may be venous, arterial or cutaneous and is fatal in 5%.

DIAGNOSIS

The probability of HIT should be assessed on clinical grounds using the following 4Ts scoring system. Heparin induced thrombocytopenia can be excluded by a low pre-test probability score without the need for laboratory testing.

<table>
<thead>
<tr>
<th>Points (0, 1, 2 for each category. Max score 8)</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td>&gt;50% fall and nadir &gt;20 (\times) 10(^9)/L</td>
<td>30-50% fall or platelet nadir 10-19 (\times) 10(^9)/L</td>
<td>Fall &lt;30% or platelet nadir &lt;10 (\times) 10(^9)/L</td>
</tr>
<tr>
<td><strong>Timing of platelet fall or other sequelae</strong></td>
<td>Clear onset between days 5-10 or (\leq 1) day if heparin within 30 days</td>
<td>Consistent with immunisation but not clear (e.g. missing count, onset after day 10 or fall (\leq 1)d if heparin 30-100d ago)</td>
<td>Platelet count fall (\leq 4) days (without recent heparin exposure)</td>
</tr>
<tr>
<td><strong>Thrombosis or other skin sequelae</strong></td>
<td>New thrombosis</td>
<td>Progressive or recurrent thrombosis</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Skin necrosis</td>
<td>Erythematous skin lesions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-heparin bolus acute systemic reaction</td>
<td>Suspected thrombosis</td>
<td></td>
</tr>
<tr>
<td><strong>Other causes for thrombocytopenia</strong></td>
<td>No other causes for platelet fall evident</td>
<td>Possible other cause present</td>
<td>Definite other cause</td>
</tr>
</tbody>
</table>

Pre-rest probability score: 6-8 = High 4-5 = Intermediate 0-3 = Low
Cardiovascular System

MANAGEMENT

Score 0-3 – LOW RISK
- Do not perform HIT assay
- Continue heparin

Score ≥4
- Stop heparin
- Start argatroban

Perform HIT ELISA (contact haematology SpR)

HIT ELISA positive
- Continue argatroban
- Observe closely for thrombosis
- Monitor platelet count

HIT ELISA negative
- Stop argatroban
- Re-start heparin

• Discuss with Haematology SpR (bleep 5886) before requesting HIT assay. Inappropriate testing and false positives make clinical management difficult.
• The test can only be run during routine working hours.

Notes
• Platelet transfusion is relatively contraindicated in HIT; discuss with a haematologist if there is a clinical concern of bleeding.
• If already anti-coagulated with warfarin, this should be stopped and reversed due to the risk of warfarin induced skin necrosis in a patient with HIT.
• Warfarin should only be restarted once platelet count has recovered (see below).
• Recovery of platelet count should be seen within 48-72 hours.

ON-GOING MANAGEMENT
• If longer term anticoagulation is not required then therapeutic anticoagulation is needed for 3 months if HIT complicated by confirmed thrombosis and 4 weeks in HIT without thrombotic complications.
• Once platelet count recovered to >100 x 10^9/L warfarin can be commenced at anticipated maintenance dose. DO NOT LOAD. See argatroban infusion protocol on next page for full instructions on converting to warfarin treatment.
ARGATROBAN INFUSION PROTOCOL

Prescribe argatroban infusion on the patient’s in-patient medication chart, as follows:

- Before prescribing argatroban check baseline coagulation screen (PT, APTT, fibrinogen) and LFTs.
- Do not use in severe liver impairment (Child-Pugh score C).

Commencing argatroban (obtain directly from pharmacy)

Prescribe initial argatroban infusion rate as directed below:

Monitoring Argatroban

Target APTT Ratio Range: 1.5 – 3.0
Check APTT ratio 2 hours after starting the infusion. Adjust dose according to the APTT ratio as follows:

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If a dose adjustment is made check the APTT ratio **2 hours** after the change is implemented.
- Continue to adjust as per protocol until APTT is in target range.
- Once in target range check APTT ratio at least daily, or if clinical situation changes.

**Converting to warfarin**

- Do not start warfarin until platelet count has recovered >100 x 10^9/L and patient has received 5 days argatroban
- Start warfarin at expected maintenance dose. **DO NOT LOAD.** Do not start with more than 5mg daily.
- Co-therapy with warfarin and argatroban will produce an additive effect on the INR. In INR ≥4 consider stopping argatroban. If infusion rate >2 micrograms/kg/min reduce to 2 micrograms/kg/min for 4-6 hours then check INR. If INR still >4 it is likely the INR on warfarin will be >2.0.
- Stop argatroban for 4 hours. Recheck INR. Argatroban must be restarted if INR <2.
2.35 Thromboembolism prophylaxis

In 2010, NICE produced Clinical Guideline 92 “Venous Thromboembolism (VTE): Reducing The Risk”. The key recommendations are:

- All patients should be assessed on admission to identify those who are at increased risk of VTE.

**VTE Risk**

- Regard **medical patients** as being at increased risk of VTE if they:
  1. have had or are expected to have significantly reduced mobility for 3 days or more or
  2. are expected to have ongoing reduced mobility relative to their normal state and have one or more of the risk factors shown in Box 1.

<table>
<thead>
<tr>
<th>Box 1 Risk factors for VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Active cancer or cancer treatment</td>
</tr>
<tr>
<td>• Age over 60 years</td>
</tr>
<tr>
<td>• Critical care admission</td>
</tr>
<tr>
<td>• Dehydration</td>
</tr>
<tr>
<td>• Known thrombophilias</td>
</tr>
<tr>
<td>• Obesity (body mass index (BMI) over 30 kg/m²)</td>
</tr>
<tr>
<td>• One or more significant medical co morbidities (for example: heart disease; metabolic, endocrine or respiratory pathologies; acute infectious disease; inflammatory conditions)</td>
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<tr>
<td>• Personal history or first-degree relative with a history of VTE</td>
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<tr>
<td>• Use of hormone replacement therapy</td>
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<td>• Use of oestrogen-containing contraceptive therapy</td>
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<tr>
<td>• Varicose veins with phlebitis</td>
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For women who are pregnant or have given birth within the previous 6 weeks see recommendations 1.6.4-1.6.6 in NICE Clinical Guideline 92.

- Regard **surgical patients** and patients with **trauma** as being at increased risk of VTE if they meet one of the following criteria:
  1. surgical procedure with a total anaesthetic and surgical time of more than 90 minutes, or 60 minutes if the surgery involves the pelvis or lower limb;
  2. acute surgical admission with inflammatory or intra-abdominal condition;
  3. expected significant reduction in mobility;
  4. one or more of the risk factors shown in Box 1.

- Assess all patients for risk of bleeding before offering pharmacological VTE prophylaxis.
Bleeding Risk

- Do not offer pharmacological VTE prophylaxis to patients with any of the risk factors for bleeding shown in Box 2 unless the risk of VTE outweighs the risk of bleeding.

- Reassess patients’ risks of bleeding and VTE within 24 hours of admission and whenever the clinical situation changes, to:
  - ensure that the methods of VTE prophylaxis being used are suitable
  - ensure that VTE prophylaxis is being used correctly
  - identify adverse events resulting from VTE prophylaxis.

**Box 2 Risk factors for bleeding**

- Active bleeding
- Acquired bleeding disorders (such as acute liver failure)
- Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR higher than 2)
- Lumbar puncture/epidural/spinal anaesthesia expected within the next 12 hours
- Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours
- Acute stroke
- Thrombocytopenia (platelets less than 75 x 10^9/L)
- Uncontrolled systolic hypertension (230/120mmHg or higher)
- Untreated inherited bleeding disorders (such as haemophilia and von Willebrand’s disease)

- Before starting VTE prophylaxis, offer patients and/or their families or carers verbal and written information.

Health Board thromboprophylaxis policy for adult inpatients

Information regarding the health board’s thromboprophylaxis policy for adult inpatients and copies of all approved thromboprophylaxis risk assessment tools, is available on the clinical portal via the link below:


Patient Information

- the risks and possible consequences of VTE
- the importance of VTE prophylaxis and its possible side effects
- the correct use of VTE prophylaxis (for example, anti-embolism stockings, foot impulse or intermittent pneumatic compression devices)
- how patients can reduce their risk of VTE (such as keeping well hydrated and, if possible, exercising and becoming more mobile).