2.1.2 CARDIAC GLYCOSIDES

- **Digoxin**  
  62.5, 125, 250 microgram tablets  
  50 micrograms/mL elixir  
  100 micrograms/mL injection (paed) (special)  
  500 micrograms/2mL injection

The dose of digoxin has to be tailored individually according to response but taking into account age, lean body weight and renal function.

**Oral Loading Dose:**

Usual Oral Loading Dose: 500 micrograms twice daily for 1 day then continue with maintenance dose.

Oral Rapid digitalisation, for atrial fibrillation or flutter: 0.75–1.5 mg over 24 hours in divided doses

*Elderly*: 250 microgram twice daily for 1 day then continue with maintenance dose.

**Oral Maintenance dose:**

*Maintenance for atrial fibrillation or flutter*, by mouth, according to renal function and initial loading dose; usual range 62.5 – 250 micrograms daily

*Maintenance for heart failure* (for patients in sinus rhythm), 62.5–125 micrograms once daily. Aim for lower digoxin levels 0.7-1 mcg/L.

In patients who are “nil by mouth”, digoxin may be given intravenously for a short period if required for rate control.

The difference in bioavailability between different digoxin formulations must be considered when changing from one dose form to another. The table below shows approximate dose equivalents.

<table>
<thead>
<tr>
<th>Tablet</th>
<th>Liquid</th>
<th>Intravenous</th>
</tr>
</thead>
<tbody>
<tr>
<td>62.5mcg</td>
<td>50mcg</td>
<td>40mcg</td>
</tr>
<tr>
<td>125mcg</td>
<td>100mcg</td>
<td>80mcg</td>
</tr>
<tr>
<td>250mcg</td>
<td>200mcg</td>
<td>160mcg</td>
</tr>
</tbody>
</table>

Dose Conversion

<table>
<thead>
<tr>
<th>0.75mg</th>
<th>750 micrograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5mg</td>
<td>1500 micrograms</td>
</tr>
</tbody>
</table>
Drug interactions

Amiodarone: levels of digoxin can be doubled by the concurrent use of amiodarone. Digoxin dose should be halved when amiodarone is added and the patient monitored closely for signs of toxicity. Levels may continue to rise for over a month.

For a full comprehensive list of other drug interactions please see the BNF or contact Medicines Information on ex 5680/1/2

Therapeutic drug monitoring:

Digoxin levels are rarely required. If levels are needed ensure steady state is achieved before taking unless there is a strong suspicion of digoxin toxicity. Blood levels should be taken at least 6 hours post dose, or immediately pre-dose. See Meditech for current dose ranges

2.2 DIURETICS

2.2.1 THIAZIDES AND RELATED DIURETICS

- **Bendroflumethiazide**  2.5mg tablets
- **Indapamide**  2.5mg tablets

2.2.2 LOOP DIURETICS

First choice

- **Furosemide**  (frusemide)

Manufacturers recommend maximum rate of injection/infusion is 4mg/min. Single doses of up to 80mg may be administered more rapidly.

**For continuous IV infusion:**

250mg made up to 50ml with sodium chloride 0.9%. Run at initial rate of 2ml/hr and adjust according to response (usual rate 0.5 - 4ml/hr). Close monitoring of U&Es is required
Second choice

- Bumetanide

### 2.2.3 POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

- Amiloride
- Spironolactone
- Eplerenone 25mg, 50mg tablets
  For initiation within 3-14 days post MI for patients with evidence of heart failure. (NICE CG48)

### 2.2.4 POTASSIUM-SPARING DIURETICS WITH OTHER DIURETICS

- Co-amilofruse 5/40 tablets
  (5mg amiloride, 40mg furosemide)

Potassium sparing diuretics should not be routinely given with a loop or thiazide diuretic. Their use is justified in:

- Patients with heart failure requiring a thiazide or loop diuretic when there is a cardiac arrhythmia or when digoxin or an anti-arrhythmic is prescribed.
- Patients with a low pre-treatment plasma potassium <3.5mmol/L.
- Patients with a concurrent condition associated with increased potassium loss.

Concomitant use of a potassium sparing diuretic and an ACE inhibitor or angiotensin II receptor antagonist should be undertaken with close monitoring to avoid hyperkalaemia. However, low dose spironolactone is commonly used in such combination in heart failure without any adverse effects.
2.2.5 OSMOTIC DIURETICS

- **Mannitol** 10%, 20% intravenous infusion
  ITU and ophthalmology only

2.3 ANTI-ARRHYTHMIC DRUGS

2.3.2 DRUGS FOR ARRHYTHMIAS

Supraventricular arrhythmias

- **Adenosine** 6mg/2mL injection

- **Digoxin** 62.5, 125, 250 microgram tablets
  50 micrograms/mL elixir
  500 micrograms/2mL injection
  100 micrograms/mL injection (paed) (special)

- **Verapamil** 40mg tablets
  120mg, 240mg m/r capsules
  5mg/2mL injection

- **Dronedarone** 400mg tablets
  For use in atrial fibrillation according to NICE TA197. Refer to Trust guidelines for further information on the management of AF.
  For Cardiologist initiation only

Supraventricular and ventricular arrhythmias

- **Amiodarone** See below for preparations and dose

- **Disopyramide** 100mg, 150mg capsules
  250mg m/r tablets

- **Esmolol** See 2.4 Beta-adrenoreceptor blocking drugs
- **Flecainide**
  50mg, 100mg tablets
  150mg/15mL injection

- **Propafenone**
  150mg tablets

- **Sotalol**
  40mg, 80mg tablets

**Ventricular arrhythmias**

- **Lidocaine**
  (lignocaine)
  0.4% (4mg/mL) in 500mL 5% glucose

- **Amiodarone**
  100mg, 200mg tablets
  150mg/3mL injection
  300mg/10mL PF syringe/Minijet

**Dose:**

**Oral:** 200mg TDS for 2 weeks then reduce to maintenance dose of 200mg od

**For rapid loading:** 400mg three times daily for 10 days then reduce to maintenance dose of 200mg od

Usual maintenance dose 200mg daily, or less if appropriate. Higher doses may be used under specialist advice.

Before initiation an ECG, LFTs, TFTs, K+ and chest X-ray must be performed.

**Drug interactions:**

There are many interactions with amiodarone. The following are some significant interactions but please consult the BNF or contact Medicines Information for advice;

**simvastatin:** Maximum dose of simvastatin that can be used with amiodarone is 20mg daily.

**flecainide:** Reduce the dose of flecainide by 50% if used concomitantly with amiodarone and monitor for adverse effects.
**digoxin:** Digoxin dose should be halved when amiodarone is added and a digoxin level taken after 1-2 weeks. Level may continue to rise for a month or more.

**phenytoin:** Phenytoin levels are raised significantly with concurrent use of amiodarone and doses should be reduced by 25-30%. Phenytoin levels should be monitored.

**warfarin:** Amiodarone increases the effect of warfarin. Reduce the dose of warfarin and monitor INR closely if amiodarone added to warfarin therapy. If commencing warfarin for patients already taking amiodarone then use lower loading doses.

Amiodarone has a half life of around 50 days but in individual patients a half life of less than 20 days and of more than 100 days has been reported. This should be taken into account, as any effects/interactions may persist for some time after amiodarone has been discontinued.

Patients newly commenced on amiodarone should be counselled before discharge.

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### 2.4 BETA-ADRENORECEPTOR BLOCKING DRUGS

- **Atenolol** 25mg, 50mg, 100mg tablets
  25mg/5mL syrup SF

- **Bisoprolol** 5mg, 10mg tablets *(angina)*
  1.25mg, 2.5mg, 3.75mg, 5mg, 7.5mg, 10mg tablets *(heart failure)*

- **Carvedilol** 3.125mg, 6.25mg, 12.5mg, 25mg, 50mg, tablets

- **Esmolol** 2500mg/250mL ready prepared infusion

- **Labetolol** 100mg, 200mg tablets
  100mg/20mL injection
• **Metoprolol** 50mg, 100mg tablets
  5mg/5mL injection

• **Sotalol** 40mg, 80mg tablets

• **Propranolol** 10mg, 40mg, 80mg tablets
  1mg/1mL injection
  80mg, 160mg capsules **m/r**

  Propranolol is generally reserved for non-cardiac indications e.g. management of migraine and prophylaxis of bleeding in portal hypertension

• **Nebivolol** 5mg tablets
  For use in heart failure

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### 2.5 HYPERTENSION AND HEART FAILURE

#### 2.5.1 VASODILATOR ANTIHYPERTENSIVE DRUGS

• **Hydralazine** 25mg, 50mg tablets

  Reserved for use in conjunction with isosorbide dinitrate for treatment of heart failure for those intolerant of other therapies (see heart failure guidelines)

#### 2.5.2 CENTRALLY ACTING ANTIHYPERTENSIVE DRUGS

• **Moxonidine** 200microgram, 300microgram, 400microgram tablets

• **Methyldopa** 125mg, 250mg, 500mg tablets
  (for use in hypertension in pregnancy)

• **Clonidine** 150microgram/mL, 1mL injection
  (ITU and theatres only)
2.5.3 ALPHA-ADRENORECEPTOR BLOCKING DRUGS

- **Doxazosin** 1mg, 2mg, 4mg tablets (OD regimen)

**NB.** Slow release (m/r, XL) doxazosin is not recommended. It is more expensive and has no advantage over the normal release preparation which has a half life of 22 hours and is therefore suitable for once daily dosing.

2.5.5 DRUGS AFFECTING THE RENIN-ANGIOTENSIN SYSTEM

2.5.5.1 Angiotensin-converting enzyme (ACE) inhibitors

- **Ramipril** 1.25mg, 2.5mg, 5mg, 10mg capsules
- **Lisinopril** 2.5mg, 5mg, 10mg, 20mg tablets
- **Perindopril** 2mg, 4mg, 8mg tablets
  
  (NB only available as *perindopril erbumine* in the strengths above)

**Perindopril** is more expensive than ramipril or lisinopril. Reserved for use post stroke, either alone or in combination with a thiazide diuretic (PROGRESS trial)

Refer to the guideline on the management of heart failure and STEMI and NSTEMI for the use of ACE inhibitors in these conditions.

See diabetes section for the use of ACE inhibitors in diabetic renal disease.

2.5.5.2 Angiotensin-II Receptor Antagonists

Angiotensin –II receptor antagonists are reserved for patients intolerant of ACE inhibitors for treatment of hypertension and diabetic renal disease.

- **Losartan** 50mg, 100mg tablets
- **Irbesartan** 75mg (initial dose in age >75 years)
  
  150mg, 300mg tablets
- **Candesartan** 2mg, 4mg, 8mg, 16mg tablets

Candesartan is reserved for patients with **heart failure** who have not had a maximum response to an ACE inhibitor or as an alternative in those who are intolerant to ACE inhibitors.
• **Valsartan**  2mg, 4mg, 8mg, 16mg tablets

Valsartan is reserved for use in the immediate post MI period in place of ACE inhibitor for patients who are known to be intolerant to ACE inhibitors. Consultant cardiologist initiation only.

**Renal function monitoring:**
Check U+Es pre-treatment then on days 3 and 7 and at months 1 and 3. Three monthly monitoring is also recommended for patients over the age of 65 years; on diuretics and/or a NSAID; with peripheral vascular disease or renal impairment.

2.5.5.3 **Renin inhibitors**

• **Aliskiren**  150mg, 300mg tablets

For consultant initiation only by renal, diabetes and cardiac physicians.

For use in patients intolerant to ACE inhibitors in intractable hypertension unresponsive to other therapies or dual renin blockade in diabetic nephropathy (unlicensed).

### 2.6  NITRATES, CALCIUM-CHANNEL BLOCKERS, AND OTHER ANTI-ANGINAL DRUGS

#### 2.6.1 NITRATES

• **Glyceryl trinitrate (GTN)**  400micrograms/dose aerosol spray

2mg buccal tablets

5mg, 10mg/24 hours transdermal patch

• **Intravenous Glyceryl trinitrate (GTN)**  50mg/50mL solution for infusion

**Administration:** Draw up 50mL into a 50mL syringe - DO NOT add any diluents. Commence infusion via syringe driver at 10mcg/min (0.6mL/hr) and titrate until a satisfactory response is achieved, headache prevents further increase in dose or the mean arterial pressure is reduced by more than 20mmHg. Measure BP after each dose adjustment and then hourly.
Caution when administering with other IV fluids and infusions. See UCL Injectable Medicines Administration Guide

- **Isosorbide dinitrate**
  - 10mg, 20mg tablets
  - For use in heart failure only (see guidelines)

- **Isosorbide mononitrate**
  - 10mg, 20mg, 40mg tablets
  - 60mg m/r tablets, capsules
  - Capsules are generally only used in primary care. However, for M/R doses of 30mg and 90mg daily, tablets must be prescribed as these may be halved.

Once daily dosing with a modified release preparation, though more expensive, may improve compliance and guarantees a nitrate free period. Immediate release isosorbide mononitrate tablets, although cheaper in Primary Care, must be taken at **8am and 6pm** to achieve a nitrate free period.

**How to prevent nitrate tolerance**

The development of tolerance and subsequent loss of clinical efficacy to nitrates during the treatment of angina and heart failure is well documented and does pose a real clinical risk.

Tolerance can be minimised by using regimens and preparations that produce a nitrate free period over several hours per day. It is not the intention with nitrate therapy to provide 24 hour cover. Other drugs should be added or doses adjusted as necessary.

The dosing regimens highlighted below minimise the risk of developing tolerance.

<table>
<thead>
<tr>
<th>preparation</th>
<th>dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glyceryl trinitrate 5mg, 10mg patches</td>
<td>Remove patch for 8 to 12 hours when patient is resting.</td>
</tr>
<tr>
<td>Glyceryl trinitrate 3mg, 5mg buccal tablet (Suscard)</td>
<td>No reports of tolerance, as Suscard Buccal has a fluctuating plasma nitrate profile. Steady state levels are achieved rapidly, and then return quickly to baseline following complete tablet dissolution after 3 to 5 hours.</td>
</tr>
<tr>
<td>Isosorbide mononitrate 60mg m/r preparations</td>
<td>Once daily</td>
</tr>
<tr>
<td>Isosorbide mononitrate 10mg, 20mg, 40mg tablets</td>
<td>Twice daily at 8am and 6pm</td>
</tr>
</tbody>
</table>
2.6.2 CALCIUM-CHANNEL BLOCKERS

- Amlodipine  5mg, 10mg tablets
- Felodipine   2.5mg, 5mg, 10mg m/r tablets
- Diltiazem    60mg m/r tablets (TDS regimen)
   (rate controlling agent) 90mg, 120mg m/r tablets or capsules (BD regimen)
   200mg, 300mg, m/r capsules (OD regimen) (this once daily dose is preferred, as it clearly distinguishes between the once and twice daily modified release preparations)

For patients already stabilised on a particular brand of a modified release diltiazem, this will continue to be supplied but there could be up to a 48 hour delay in obtaining these. When a patient’s dosage of diltiazem is altered during an in-patient stay, the Pharmacy department will usually supply whichever is the contract brand at that time.

- Verapamil    40mg tablets
   (rate controlling agent) 120mg m/r tablets
   240mg m/r tablets
   5mg/2mL injection

Calcium channel blockers should be used with caution in patients with evidence of impaired left ventricular function. If a calcium channel blocker must be used then amlodipine is considered to be the safest option.

- Nimodipine  30mg tablets
   10mg/50mL intravenous infusion

Nimodipine is reserved for prevention of vascular spasm following aneurysmal subarachnoid haemorrhage. **It is NOT recommended following traumatic subarachnoid haemorrhage.**

2.6.3 OTHER ANTIANGINAL DRUGS

- Nicorandil  10mg, 20mg tablets
- Ivabradine  5mg, 7.5mg tablets
To be initiated by cardiologists only.
See NICE guidance TA267 Ivabradine for treating chronic heart failure

- **Ranolazine**
  375mg, 500mg, 750mg tablets
  Last line for stable anginal patients only, when they are already on maximum doses of all other anti-anginals or they have a SBP $\leq 100$ or HR $\leq 60$ bpm which limits the use/dose escalation of other agents.

  To be initiated by consultant cardiologists only.

### 2.6.4 PERIPHERAL VASODILATORS AND OTHER DRUGS

- **Naftidrofuryl oxalate**
  100mg capsules
  Reserved for the specific indication only for the treatment of intermittent claudication in people with peripheral arterial disease in according to NICE TA223

### 2.7 SYMPATHOMIMETICS

#### 2.7.1 INOTROPIC SYMPATHOMIMETICS

- **Dobutamine**
- **Dopamine**
- **Isoprenaline**

### 2.8 ANTICOAGULANTS AND PROTAMINE

#### 2.8.1 PARENTERAL ANTICOAGULANTS

**Heparin**
Intravenous preparations
- **Heparin sodium**
  - 5000 units/5mL
  - 20,000 units/20mL

**Low Molecular Weight Heparins (LMWH)**

- **Enoxaparin**
  - 100mg/mL
  - pre-filled syringes:
    - 20mg in 0.2mL
    - 40mg in 0.4mL
    - 60mg in 0.6mL
    - 80mg in 0.8mL
    - 100mg in 1mL

  Enoxaparin is currently only used in the Trust for the treatment of Non ST-segment-elevation Myocardial Infarction.

  Tinzaparin is the LMWH of choice and should be used in all other instances where a LMWH is indicated.

- **Tinzaparin**
  - 20,000units/mL
  - pre-filled syringe:
    - 10,000units in 0.5ml
    - 14,000units in 0.7ml
    - 18,000units in 0.9mL
  - 20,000units/mL
  - vial:
    - 40,000units in 2ml

**Air bubbles and LMWH syringes**

When the total contents of a syringe containing a LMWH is required to be administered inject the whole contents of the syringe including the air bubble. The subcutaneous injection of a small amount of air with the syringe contents has no clinical significance. Removing the air bubble may lead to a significant reduction in the dose administered.

When a proportion of a syringe is required for a dose, the excess heparin and the air bubble should be expelled from the syringe. This should be done by holding the syringe vertically with the needle uppermost and allowing the air bubble to float to beneath the needle before expelling the air and then the excess heparin. Try to keep the outside of the needle free from liquid, as wet needles have been thought to be responsible for some injection complications.

**Fondaparinux**

- **Fondaparinux sodium**
  - 2.5mg (0.5mL) pre-filled syringe
For use in the management of Acute Coronary Syndrome – NSTEMI see guidelines.

Fondaparinux may also be used in place of unfractionated heparin or LMWH for treatment and prophylaxis of DVT/PE in patients where the use of heparins is inappropriate or contraindicated for example following the development of or in patients prone to heparin induced thrombocytopaenia. Please consult Haematologist or Medicines Information for further advice.

**Heparinoids**

- **Danaparoid** 750units/0.6mL injection

**heparin flushes**

- **Heparin sodium**
  - 200units/2mL
  - 50units/5mL

Sodium chloride 0.9% should be used to flush peripheral catheters since there is no evidence to suggest it is less effective than heparin. Sodium chloride 0.9% may be administered without a prescription when it is being used as a flushing solution and to check or maintain the patency of intravenous catheters in line with the Trust’s flushing and cannulation policy guidelines. **Heparin flushes are expensive and should only be used to maintain the patency of central venous catheters. They MUST be prescribed.**

### 2.8.2 ORAL ANTICOAGULANTS

First choice

- **Warfarin** 1mg, 3mg tablets

**Warfarin anticoagulant monitoring charts**

These charts are to be used to record the monitoring and doses of warfarin to be administered. Each chart should be completed with all patient details (use an addressograph sticker) including the reason for the use of warfarin, target INR and duration of therapy. This information is important as a copy of the chart is sent to the patient’s General Practitioner on discharge.
Warfarin should continue to be prescribed on EP or the prescription chart in non-EP areas.

Guidelines for the initiation, dosing and monitoring of warfarin are available on the hospital intranet or on the anticoagulant prescription charts and referral forms.

NB Please check the BNF or with the Haematologists or Pharmacists for advice on warfarin drug interactions.

Apixaban: the RAG classification for apixaban depends on the indication

- **Apixaban**  
  Apixaban is the preferred choice in COCH for VTE prophylaxis following elective hip and knee replacement.
  
  Elective total knee replacement 2.5mg twice daily for 10 days
  
  Elective hip replacement 2.5mg twice daily for 35 days
  
  **NB The total course of treatment must be prescribed on discharge and supplied from the hospital pharmacy.**
  
  Please see [NICE TA245](#)

- **Apixaban**  
  For the prevention of stroke and systemic embolism in atrial fibrillation as per [NICE TA275](#)

Dabigatran: the RAG classification for dabigatran depends on the indication

- **Dabigatran**  
  For the prevention of stroke and systemic embolism in atrial fibrillation: as per [NICE TA249](#)

- **Dabigatran**  
  For primary prevention of venous thromboembolic events in adults who have undergone elective total hip replacement surgery or elective total knee replacement surgery (as per [NICE TA157](#))

Rivaroxaban: the RAG classification for rivaroxaban depends on the indication

- **Rivaroxaban**  
  For the prevention of stroke and systemic embolism in atrial fibrillation:
as per NICE TA256

- Rivaroxaban As an option for treatment of DVT and long term prevention of VTE for those patients who have already been diagnosed with a DVT in accordance with NICE TA261

- Rivaroxaban For primary prevention of venous thromboembolic events in adults who have undergone elective total hip replacement surgery or elective total knee replacement surgery (as per NICE TA170)

For further information see Joint COCH/Western Cheshire Guidelines on the Treatment Strategy and Thromboprophylaxis in AF

### 2.8.3 PROTAMINE

- Protamine 50mg/5mL injection

### 2.9 ANTIPLATELET DRUGS

- Aspirin 75mg, 300mg dispersible tablets

Aspirin is considered as first line antiplatelet except in specific indications (eg stroke) or in case of aspirin hypersensitivity or true aspirin intolerance as defined below:

- If gastrointestinal symptoms develop while taking low dose aspirin, a review of drug therapy and lifestyle should be undertaken. Factors such as excess alcohol and concomitant therapy with an NSAID should be managed before attributing symptoms of aspirin. If gastrointestinal symptoms persist, addition of a PPI i.e. lansoprazole 15-30mg daily should be the next option.

- In those rare patients with gastrointestinal problems not controlled by these measures or intolerant to aspirin for other reasons e.g. definite, proven allergy, clopidogrel 75mg may be used. A past medical history of a peptic ulcer or previous GI bleeding that has now healed should not mean that the patient is started on clopidogrel. The same applies to previous
reports of aspirin ‘intolerance’ that have not been managed by the simple measures outlined above. Aspirin should be started in the first instance and should gastrointestinal symptoms occur the patient should be reviewed as before.

- **Clopidogrel** 75mg tablets
- **Dipyridamole** 200mg m/r capsules

Refer to NICE TA210 for the use of clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events

**Clopidogrel interactions**

There has been a number of studies published suggesting a potential interaction between clopidogrel and drugs that inhibit the liver enzyme CYP2C19. This interaction may result in clopidogrel being less efficacious and increase the risk of major cardiovascular events such as stroke/TIA, ACS, CV death or coronary revascularisation.

The Western Cheshire Area Prescribing Committee has issued local guidance on the interaction between clopidogrel and PPIs, and clopidogrel and fluoxetine, two commonly prescribed inhibitors of CYP2C19. Please consult each product’s SPC for a full list of interactions.

- **Prasugrel** 5mg, 10mg tablets

For patients undergoing PCI in accordance with NICE TA182

- **Ticagrelor** 90mg tablets

In combination with aspirin for the prevention of atherothrombotic events in patients with acute coronary syndrome, in accordance with NICE TA236

- **Tirofiban** 50micrograms/mL infusion 250mL

The use of this drug for ‘Acute Coronary Syndrome’ is restricted to the Coronary
See NICE TA47 Glycoprotein IIb/IIa inhibitors in acute coronary syndrome (partially updated by NICE CG94)

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2.10 STABLE ANGINA, ACUTE CORONARY SYNDROMES, AND FIBRINOLYSIS

2.10.2 FIBRINOLYTIC DRUGS

- **Tenectaplaste**  
  See local/pathways for management of chest pain and ACS  
  See NICE TA52 for information on use of drugs for thrombolysis

- **Alteplase**  
  For Stroke (acute, ischaemic) see NICE TA264 guidance.

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2.11 ANTIFIBRINOLYTIC DRUGS AND HAEMOSTATICS

- **Tranexamic acid**  
  500mg tablets  
  500mg/5mL injection

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2.12 LIPID-REGULATING DRUGS

The Joint Lipid Guidelines for the Countess of Chester NHS Foundation Trust and Western Cheshire PCT can be found here

In addition see NICE TA94 Statins for the prevention of cardiovascular events.

**Statins**

- **Simvastatin** 40mg tablets *(First line)*
- **Pravastatin** 40mg tablets
First line if simvastatin not tolerated or taking drugs which interact with simvastatin. See guidelines

- **Atorvastatin**  
  40mg, 80mg tablets  
  **First line for post ACS only**  
  For all other indications refer to guidelines

**Fibrates**

- **Bezafibrate**  
  200mg m/r tablets

- **Fenofibrate**  
  67mg, capsules  
  (micronised)  
  160mg m/r tablets

**Other agents**

- **Colestyramine**  
  4g sachet

- **Ezetimibe**  
  10mg tablets  
  See [NICE TA132](https://www.nice.org.uk/guidance/ta132) Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia

- **Omacor**  
  1g capsule  
  For initiation post MI only, secondary to lifestyle and diet interventions as per [NICE CG48](https://www.nice.org.uk/guidance/cg48)  
  See section 2.10 for local guidelines and Omacor Initiation Pathway
Joint Lipid Guidelines

NICE has published clinical guidelines on lipid modification for the primary and secondary prevention of cardiovascular disease (CVD) (CG 67), the management of familial hypercholesterolaemia (CF71) and in the management of type 2 diabetes (CG 87).

1. Primary prevention (CG 67)

Patients aged 75 years or over are high risk, so can be offered a statin without risk assessment.

Optimise management of other modifiable risk factors before offering lipid-regulating drugs.

Patients aged 40-74 years should have a risk assessment of CVD using an appropriate risk assessment tool.
If greater than 20% offer statin therapy.
N.B. If using Framingham, pay attention to factors that increase the risk e.g. family history and South Asian men.

Offer simvastatin 40mg nocte.
If this is not tolerated or there are contraindications or potential drug-drug interactions, a lower dose of simvastatin or pravastatin 40mg should be used (see general advice at end).
Higher intensity statins or nicotinic acid should not be used.
Do not offer the combination of an anion exchange resin, fibrate or fish oil supplement with a statin.

If statins are not tolerated consider fibrates, ezetimibe or anion exchange resins.

Monitoring of lipid levels is not necessary as there are no target levels for primary prevention.
Measure liver function within 3 months of starting statin therapy and at 12 months, but not again unless clinically indicated
Check compliance with therapy and lifestyle changes at every review.
If initiating simvastatin in patients taking warfarin, monitor INR frequency until stable.
2. Secondary prevention (CG 67)

- Acute Coronary Syndrome
  - Atorvastatin 80mg od for 6 months then review as below

- Other secondary prevention
  - Post STEMI
  - Other ischaemic heart disease
  - Peripheral vascular disease
  - Cerebrovascular disease (ischaemic stroke/TIA)

Prescribe simvastatin 40mg noecte. If not tolerated / interacting drugs give a lower dose or pravastatin 40mg (see general information at end). If unable to tolerate any statin at low dose consider ezetimibe, fibrates, nicotinic acid or resins.

Monitor lipids and LFTs at 3 months and 12 months. Check lipids annually.

Where TC remains >4.0 mmol/L OR LDL-C >2.0 mmol/L on simvastatin 40mg (after checking compliance), consider increasing to simvastatin 80mg or a drug of similar efficacy and acquisition cost. Any decision to offer a higher intensity statin should take into account informed preference, co-morbidities, multiple drug therapy and the potential benefits and risks of treatment. Atorvastatin 40mg is third line choice and should only be used after an adequate trial of simvastatin at both 40mg and 80mg doses.

The audit level is TC<5mmol/L. NICE recognises that more than 50% of patients will not achieve a TC<4mmol/L or LDL-C<2mmol/L and state that it is not cost effective to titrate treatment above simvastatin 80mg noecte.
### 3. Diabetes mellitus (CG 87)

#### Under 40

- **Is patient at high risk? i.e.**
  - Features of metabolic syndrome
  - Other CV risk factors
  - Microalbuminuria
  - At-risk ethnic group
  - Family history of premature CVD

- **No**
  - Reassess Annually

- **Yes**
  - Perform a diabetes lipid profile (NOT FASTING) then start simvastatin 40mg noce (pravastatin 40mg if contra-indicated or not tolerated)
  - Review lipids and LFTs after 3 months
  - **Target lipid Levels:**
    - TC < 4mmol/L OR LDL-C < 2mmol/L

- **Target lipid levels achieved:**
  - Continue
  - Monitor diabetic lipid profile and LFTs again in 12 months
  - Check lipids annually

- **Target not achieved**

#### Over 40

- **Is patient at low risk? i.e.**
  - BMI within ideal range
  - BP < 140/80mmHg (untreated)
  - No microalbuminuria
  - No hyperlipidaemia
  - No CVD
  - No family history of CVD
  - Non smoker

- **No**
  - Calculate CVD risk using UKPDS Risk Engine (www.dtu.ox.ac.uk)

- **Yes**
  - ≥20% over 10 years
  - <20% over 10 years
  - Reassess annually

#### Professional Guidance

**Consider:**
- Simvastatin 80mg
- Atorvastatin 40mg (if increased albumin excretion rate or existing/newly diagnosed CVD)
- Addition of ezetimibe
- If TGs = 2.3 – 4.5mmol/L despite statin, consider adding fibrate
- Fibrate may be 1st line if TGs > 4.5mmol/L. See formulary for choice
- Specialist advice

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To avoid the risk of hypoglycaemia the local diabetes team recommend that ALL patients with diabetes have a NON-FASTING SAMPLE (irrespective of their diabetes treatment). If "Diabetes Lipids (non-fasting)" is requested (via the ICE Desktop) the Countess laboratory will automatically measure Total and HDL-Cholesterol, if "DAR" is requested U&Es, random Glucose and HbA1c will be added.

Joint Lipid Guidelines Version 1.0 August 2010  Review date August 2012
4. Familial hypercholesterolaemia (FH) (CG 71)

The possibility of FH should be considered if:
- Total cholesterol >7.5mmol/L or LDL-C >4.9mmol/L (adult)
- Total cholesterol >6.7mmol/L or LDL-C >4.0mmol/L (<16yrs)

Exclude secondary causes:
- E.g. Thyroid disease / diabetes mellitus / drug effects / lifestyle

Review lipids and ALT again after 2-3 months.

If TC still >7.5mmol/L or LDL-C >4.9mmol/L (adult)
- >6.7mmol/L or LDL-C >4.0mmol/L (<16 years)

PLUS

Either
- Family history of early onset CVD
  i.e First degree relative below 60 years
    Second degree relative below 50 years

- Do not calculate CVD risk
- Refer to specialist service such as the Lipid Clinic. Start on simvastatin 40mg nocte unless referral is made promptly.
General Advice

Blood tests
All patients should have glucose, U&E, LFT, creatine kinase (CK) and TSH checked before starting a statin.

In primary prevention / suspected familial hypercholesterolaemia, treatment should not be started on the basis of one fasting lipid profile. It is reasonable to give lifestyle advice and repeat bloods and risk assessment after a further fasting test 2-3 months later.

In secondary prevention the statin should be started without waiting for a lipid measurement.

In secondary prevention it is appropriate for fasting lipid levels to be checked at 3 months after a statin is initiated and then annually. Lipid levels do not need to be checked for primary prevention.

Diabetics should have a non-fasting lipid test.

There is no need to routinely test CK levels in asymptomatic patients.

LFTs should be measured in both primary and secondary prevention at the start of treatment, at 3 months and at 12 months. They do not need to be measured thereafter unless clinically indicated. Patients with a transaminase (ALT / AST) level <3x ULN can continue a statin. If ALT increases to >3x ULN during treatment, continue treatment but repeat test after one month. If ALT remains >3x ULN at that stage withdrawal of treatment may be required but consideration should also be given to the use of a lower dose or use of a different statin.

Cautions
Concurrent diseases/conditions which indicate caution should be used include: renal impairment, myalgia, rhabdomyolysis, myositis, raised liver enzymes, liver disease, diabetes with evidence of hepatic fatty changes, heavy exercise, excessive alcohol intake, debilitated status or trauma, ischaemia reperfusion and pancreatitis.
Discontinue statin if peripheral neuropathy develops.

Contraindications
Pregnancy and lactation. Women of reproductive age, who are on statins, should be instructed to stop their treatment 3 months before any attempt to conceive.
### Drug Interactions

<table>
<thead>
<tr>
<th>Interacting drug or food</th>
<th>Simvastatin prescribing advice</th>
<th>Atorvastatin prescribing advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potent CYP3A4 inhibitors, including itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin, and HIV protease inhibitors</td>
<td>All are contraindicated with simvastatin</td>
<td>Avoid if possible: consider temporary suspension of atorvastatin if interacting drug is taken for short period <strong>Itraconazole</strong>: do not exceed 40mg atorvastatin daily <strong>Clarithromycin</strong>: do not exceed 20mg atorvastatin daily <strong>HIV protease inhibitors</strong>: Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used</td>
</tr>
<tr>
<td>Ciclosporin*</td>
<td>Do not exceed 10mg simvastatin daily</td>
<td>Do not exceed 10mg atorvastatin daily</td>
</tr>
<tr>
<td>Danazol</td>
<td>Do not exceed 10mg simvastatin daily</td>
<td>No restriction in Summary of Product Characteristics</td>
</tr>
<tr>
<td>Verapamil, Amiodarone</td>
<td>Do not exceed 20mg simvastatin daily</td>
<td>Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Do not exceed 40mg simvastatin daily</td>
<td>Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used</td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td>Avoid grapefruit juice</td>
<td>Limit intake of grapefruit juice to very small quantities (or avoid altogether)</td>
</tr>
<tr>
<td>Warfarin/coumarins†</td>
<td>Monitor INR before starting treatment and regularly during treatment, especially with dose changes</td>
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</tr>
<tr>
<td>Fibrates†</td>
<td>Increased risk of myopathy when used with fibrates; do not exceed 10mg simvastatin daily (except with fenofibrate); gemfibrozil increases systematic exposure to simvastatin</td>
<td>Increased risk of myopathy when used with fibrates; gemfibrozil increases systematic exposure to atorvastatin</td>
</tr>
<tr>
<td>Ezetimibe†</td>
<td>Additive risk of myopathy cannot be ruled out</td>
<td>Additive risk of myopathy cannot be ruled out</td>
</tr>
</tbody>
</table>

* Ciclosporin interacts with all statins and is contraindicated with rosuvastatin
† Warfarin/coumarins, fibrates and ezetimibe are important potential interactions to consider for all statins

Drug interaction table from MHRA Drug Safety Update Volume 1 Issue 6 January 2008

SPCs for atorvastatin and simvastatin state that if concomitant treatment with an interacting potent CYP3A4 inhibitor (as in table above) is unavoidable, therapy with statin should be suspended during the course of treatment.

See BNF for full list of interactions