## Asthma Pathway and Prescribing Policy for Adults in Primary and Secondary Care with Costs

### Diagnosis
- Clinical history (exacerbations)
- Peak flow variability
- Triggers

### Treatment Options
- **Step 1**
  - Salbutamol 100mcg MDI + spacer PRN (200 doses £1.50)
  - Salbutamol 100mcg Easyhaler PRN (200 doses £3.31)
  - Salbutamol 100mcg Easi-Breathe PRN (200 doses £6.30)
  - Terbutaline 500mcg Turbohaler PRN (100 doses £6.92)
  - Salbutamol 200mcg Accuhaler (60 doses £3.00)

- **Step 2**
  - Qvar Easi-Breathe 50mcg 2 puffs BD (£57 p.a)
  - Clenil Modulite MDI 100mcg 2 puffs BD + spacer (£59 p.a)
  - Budesonide Easyhaler 100mcg 2 puffs BD (£65 p.a)
  - Fluticasone MDI 50mcg 2 puffs BD + spacer (£71 p.a)
  - Budesonide Turbohaler 100mcg 2 puffs BD (£86 p.a)
  - Fluticasone Accuhaler 100mcg 1 puff BD (£109 p.a)

- **Step 3**
  - DuoResp Spiromax 160/4.5 1 puff BD (£182 p.a)
  - Fostair MDI 100/6 1 puff BD + spacer (£183 p.a)
  - Seretide Accuhaler 100 1 puff BD (£219 p.a)
  - Seretide MDI 50 2 puffs BD + spacer (£224 p.a)
  - Flutiform MDI 50/5 2 puffs BD + spacer (£224 p.a)
  - Symbicort Turbohaler 200/6 1 puff BD (£231 p.a)

- **Step 4**
  - Fostair MDI 100/6 2 puffs BD + spacer (£362 p.a)
  - Flutiform MDI 125/5 2 puffs BD + spacer (£361 p.a)
  - DuoResp Spiromax 160/4.5 2 puffs BD (£365 p.a)
  - Seretide Accuhaler 250 1 puff BD (£426 p.a)
  - Seretide MDI 125 2 puffs BD + spacer (£431 p.a)
  - Symbicort Turbohaler 200/6 2 puff BD (£462 p.a)

  **Consider adding:**
  - Leukotriene antagonist montelukast 10mg od (£29 p.a)
  - Theophylline

- **Step 5**

### Monitoring
- At each step assess:
  - Inhaler technique
  - Compliance
  - Control
  - Smoking

### Step Down
- If well controlled, step down and reassess at 3-6 months

- Poor symptom control
- Nighttime symptoms
- Significant peak flow variability

### Referral to Secondary Care
- All patients at step 5
- Selected patients at step 4 according to GP expertise

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Specific recommendations for asthma patient care

1. Patients should be managed according to the British Thoracic Society guidelines stepwise approach. The guideline is represented in the accompanying flowchart.

2. Only the inhalers listed should be used. The cost of each inhaler is shown. For short acting bronchodilators the costs are according to each unit, and the number of doses per unit included. For inhaled steroids and combination inhalers, the cost per annum is shown according to the dosing schedule. Where a spacer device is advised for steroids and combination inhalers, the cost of one spacer device per annum has been included.

3. Patients who require a step up in therapy should be reviewed at 3-6 months and step down considered.

4. Inhaler technique should be checked regularly by all trained health professionals. Patients using dry powder inhaler devices (Turbohalers, Easyhalers, Accuhalers and Spiromax) should have their inspiratory flow measured with an In-Check device to ensure that flow rates of 30-90 l/min can be achieved.

5. Metered dose inhaler devices (MDIs) should only be prescribed with a large or medium volume spacer.

6. Failure to control patients at step 4 should trigger a referral to secondary care. This includes patients using more than the stated inhaler dose at step 4 in the flowchart (e.g. SMART regime).

7. Smokers should be offered nicotine replacement therapy and referral to a smoking cessation programme at every opportunity.

Supporting information

1. Dose equivalence of inhaled corticosteroids:

<table>
<thead>
<tr>
<th>Inhale</th>
<th>Micrograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clenil (beclometasone)</td>
<td>200</td>
</tr>
<tr>
<td>Qvar* (beclometasone)</td>
<td>100</td>
</tr>
<tr>
<td>budesonide</td>
<td>200</td>
</tr>
<tr>
<td>fluticasone propionate</td>
<td>100</td>
</tr>
<tr>
<td>beclometasone* as Fostair</td>
<td>80</td>
</tr>
</tbody>
</table>

*the beclometasone in Qvar and Fostair has extra-fine particles and is more potent than Clenil Modulite.


3. Prices are taken from the eMC Dictionary of Medicines and Devices (accessed January 2015) and may change.

4. The cost of a large volume spacer (Volumatic) is £3.81 and a medium volume spacer (Aerochamber Plus) is £4.79.
Cardiff and Vale UHB Medicines Management Group
Inhaled Corticosteroid Task and Finish Group

Aims
1. To improve asthma and COPD care in primary and secondary care by providing clear and easy to use guidelines
2. To harmonise the management of asthma and COPD between primary and secondary care resulting in improved outcomes for patients, in particular a reduction in exacerbations and hospital admissions
3. To rationalise inhaler therapy, reduce unnecessary prescribing and deliver significant cost savings across the health board.

Asthma

Background
Asthma is a chronic inflammatory condition of the airways characterised by exacerbations. A meta-analysis has demonstrated that 90% of the therapeutic benefit of steroids can be achieved with a total daily dose of fluticasone of 100-250mcg\(^1\) (equivalent to a total daily dose of beclometasone or budesonide of 200-500mcg). However, studies of local inhaler prescribing in primary care have suggested that in many patients much higher doses of inhaled steroids are prescribed. British thoracic society asthma guidelines delineate a stepwise approach to asthma management and highlight that patients who are well controlled should be stepped down and reviewed\(^2\). We believe that in many cases this does not occur, resulting in unnecessary inhaler prescription.

Poor control of asthma is often due to poor compliance with treatment and also poor inhaler technique. Studies of metered dose inhaler (MDI) devices have demonstrated poor technique, even after training\(^3\). Other factors associated with poor control include poor education about the disease process and exposure to asthma triggers, especially cigarette smoke.

References
3. Hardwell A, Barber V, Hargardon T et al. Technique training does not improve the ability of most patients to use pressurised metered dose inhalers (pMDI). Prim Care Resp J 2011; 20(1) 92-96

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November 2011

Review date: January 2016.
**COPD PATHWAY AND PRESCRIBING POLICY FOR ADULTS IN PRIMARY AND SECONDARY CARE WITH COSTS**

**Diagnosis**
- Smoking history (>20 pack years), breathlessness and exacerbations
- Obstructive spirometry (mandatory for a diagnosis - see notes)

**SABA options:**
- salbutamol 100mcg MDI + spacer PRN (200 doses £1.50)
- salbutamol 100mcg Easyhaler PRN (200 doses £3.31)
- salbutamol 100mcg Easi-Breathe PRN (200 doses £6.30)
- terbutaline 500mcg Turbohaler PRN (100 doses £6.92)
- salbutamol 200mcg Accuhaler (60 doses £3.00)

**SAMA**
- ipratropium 20mcg MDI + spacer PRN (200 doses £5.56)

**LABA options:**
- formoterol Easyhaler 12mcg 1 puff BD (£144 p.a)
- formoterol Turbohaler 12mcg 1 puff BD (£302 p.a)
- salmeterol Accuhaler 50mcg 1 puff BD (£356 p.a)
- salmeterol MDI 25mcg 2 puffs BD + spacer (£361 p.a)

**LAMA options (stop SAMA):**
- glycopyrronium Breezhaler® 1 puff OD (£335 p.a)
- aclidinium Genuair® 1 puff BD (£348 p.a)
- tiotropium Respimat® 2.5mcg 2 puffs OD (£408 p.a)
- tiotropium Handihaler 18mcg 1 puff OD (£409 p.a)

**Combination LABA and ICS options:**
- First line
  - Symbicort Turbohaler 400/12 1 puff BD (£462 p.a)
- Second line
  - Relvar Ellipta 92/22 1 puff OD (£338 p.a)
  - Fostair MDI 100/6 2 puffs BD (£362 p.a)
  - DuoResp Spiromax 320/9 1 puff BD £365 p.a)
  - Seretide Accuhaler 250 1 puff BD (£426 p.a)

**Mucolytic:**
- carbocisteine 750mg BD (£213 p.a.)

**FEV₁ ≥50%**
- LABA
- LAMA

**FEV₁ <50%**
- LABA + ICS combination
- LAMA + LABA + ICS

**Referral to secondary care**
- diagnostic uncertainty
- oxygen saturations <93%
- acute deteriorations
- pulmonary rehabilitation
- new CXR changes or haemoptysis (urgent ref)

**Inhaler technique**
- check inhaler technique and compliance at every opportunity

**Smokers**
- ask about smoking at every opportunity and refer to smoking cessation services

**Preparation date:** Dec 2011. **Updated:** Mar 2015. **Review date:** Mar 2016
Specific recommendations for COPD patient care

Diagnosis

Spirometry is mandatory to make a diagnosis as the majority of smokers will not develop clinically significant COPD. As part of normal aging, lungs lose elasticity and the FEV₁/FVC ratio reduces with age. A more reliable measure than using a fixed ratio of <0.7 is to define airways obstruction as an FEV₁/FVC ratio of less than the lower limit of normal (less than the bottom 5% of normally distributed values). In practice the normal FEV₁/FVC ratio range at different ages is 0.6-0.8 so any value <0.6 always indicates airways obstruction. The severity of airways obstruction is determined by the percentage predicted FEV₁.

NICE 2010 COPD severity

<table>
<thead>
<tr>
<th>FEV₁</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30%</td>
<td>very severe</td>
</tr>
<tr>
<td>30-50%</td>
<td>severe</td>
</tr>
<tr>
<td>50-80%</td>
<td>moderate</td>
</tr>
<tr>
<td>&gt;80%</td>
<td>mild (requires symptoms to be significant)</td>
</tr>
</tbody>
</table>

Management

1. Stopping smoking is the key intervention in COPD. Smoking should be addressed at every opportunity and referral made to smoking cessation services.
2. Treatment with pharmacotherapy is indicated in COPD patients with exacerbations and/or persistent dyspnoea.
3. Patients still breathless despite SABA or SAMA should be tried initially with formoterol easyhaler which is the cheapest option.
4. Failure to improve symptomatically on either LABA or LAMA should result in the drug being stopped and an alternative tried.
5. Tiotropium handihaler is recommended as the first line LAMA as there is more long-term outcome and safety data than with the newer agents (aclidinium and glycopyrronium). Aclidinium genuair, glycopyrronium breezhaler and spiriva respimat are second line options for patients where spiriva handihaler is not suitable (e.g. unable to use device, intolerable side effects).
6. The combination inhaler choices are those providing total doses of 800-1000mcg of beclometasone equivalent/day, i.e. budesonide 800mcg/day and fluticasone 500mcg/day. Although some of these devices and doses are off-license, this decision has been taken in the light of recent evidence demonstrating an increased risk of pneumonia with inhaled corticosteroids in COPD.
7. Inhaled corticosteroid/LABA combination should be used in frequent exacerbators (more than 2 per annum) with FEV₁<50%. They can be considered in frequent exacerbators, particularly when these are associated with hospital admissions even when FEV₁>50%.
8. Symbicort (budesonide/formoterol) is recommended as the first line inhaled corticosteroid/LABA combination in view of the recently published PATHOS study. Budesonide/formoterol was associated with fewer exacerbations, fewer COPD-related hospitalisations and a lower risk of pneumonia when compared to seretide (fluticasone/salmeterol).
9. Only prescribe carbocisteine in those with chronic sputum production and reduce to BD maintenance dose.
10. Check inhaler technique and use In-Check device to ensure flow rates 30-90 L/minute for all dry powder devices. MDI’s must be prescribed with a spacer.

Good Prescribing Guide

Prescribing Guidelines for Medical Staff

Seventh Edition
April 2014
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How to use this Guide

This Good Prescribing Guide updates the sixth edition of the Good Prescribing Guide for Cardiff and Vale UHB, which was published in January 2011. In addition to updated or new material, NICE and National Service Framework Guidance have been incorporated where appropriate. The first edition of the Guide was based on prescribing guidelines from the Integrated Medicine Directorate and this work is gratefully acknowledged.

The Guide is intended to supplement the British National Formulary and Cardiff and Vale UHB Formulary (INFORM) and to provide information on evidence-based local practices within the UHB.

The guidelines are intended for adult use only. The Department of Child Health in Cardiff and the Vale of Glamorgan produce Clinical Guidelines for use in paediatrics.

Guidelines are indexed by BNF category for ease of cross-reference.

Only drugs in the hospital formulary should be initiated.

If you have any comments on existing guidelines or suggestions for topics which should be included please contact a member of the Good Prescribing Guide Steering Group.

This information is issued on the understanding that it is the best available from the resources at our disposal at the date of compilation.

The Good Prescribing Guide Steering Group gratefully acknowledges the work of those people who either contributed to and/or commented on various sections of the Guide.

An electronic version of the Good Prescribing Guide is available on the Cardiff and Vale Intranet/Clinical Portal Homepage/Clinical Support Service/Pharmacy/Clinical Guidance/ Good Prescribing Guide and via the Welsh Medicines Information Centre website www.wmic.wales.nhs.uk. This will be updated as new guidance becomes available and agreed and therefore may contain more up to date information than the printed copy.

Seventh Edition
January 2014
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PALLIATIVE CARE

Contact numbers for Palliative Care Team (PCT):
UHW Ext 43377 or UHL Ext 25196 or bleep doctors or nurses via switchboard

Out of hours Contact:
Sat & Sun 9am - 5pm bleep Clinical Nurse Specialist via switchboard.
24/7 advice from Holme Tower Marie Curie Hospice (029 20426000).

i) Pain assessment
Consider cause and type of pain(s)

1. Visceral Pain
Usually described as dull, aching constant pain which is poorly localised.
Treat following WHO Analgesic Ladder using regular oral analgesia in a stepwise fashion.

- Mild pain: non-opioids e.g. paracetamol, NSAIDS if no contra-indications.
- Moderate pain: weak opioids e.g. codeine, dihydrocodeine
  Two strengths of combined paracetamol/codeine preparations exist;
  co-codamol 8/500,
  co-codamol 30/500
- Severe pain: strong opioids e.g. morphine, oxycodone, fentanyl
  (see section iii)

2. Bony Pain
Usually easily localised and exacerbated by movement and often associated with local tenderness. Treat according to WHO Analgesic Ladder as above and consider role of palliative radiotherapy. If background pain is well-controlled, but pain occurs secondary to movement or weight-bearing (called ‘incident pain’), then a prophylactic short-acting opioid may be prescribed pre-emptively with advice from PCT.

If bony pain relates to the spine, always have a high index of suspicion for spinal cord compression (SCC) and urgently investigate (MRI) and treat (nurse flat, start high dose steroids pre-scan) and seek urgent spinal surgical opinion if SCC confirmed.

Clinical assessment of risk of pathological fracture is important; if this is a concern, discuss with Orthopaedic Teams.

3. Neuropathic Pain
This is described as sharp, lancinating, burning pain which is often associated with altered light touch, hyperalgesia, allodynia, or pain that is in a dermatomal distribution.
Treat according to WHO Analgesic Ladder.
Adjuvant analgesics include:
Palliative Care

- Amitriptyline 10-25mg nocte increasing up to 75mg nocte
  OR
- Gabapentin initially at 300mg daily increasing gradually up to 1800mg a day
  (see also section 4.4)

**ii) Prescribing strong opioids**

**Oral morphine is the opioid of first choice** (e.g. Sevredol tablets or Oramorph liquid if patients are unable to swallow tablets or morphine dose is less than 5mg)

If changing from full dose weak opioid (8 tablets of co-codamol 30/500 per day)

Stop co-codamol 30/500
- Start with oral morphine 10mg every 4 hours.
- Also prescribe oral morphine 10mg prn hourly.

Where regular weak opioids have not been used or in elderly patients:
- Start with oral morphine 2.5mg every 4 hours or 5mg if co-codamol 30/500 has been used prn.

**Review patient’s response every 24 hours after starting strong opioids;**

If patient is still in pain increase opioid dose by 30-50% every 24 hours until pain controlled.

i.e. increase oral morphine from 5 → 7.5 → 10 → 15 → 20 → 30mg

**When pain is controlled:**
Consider converting to slow release morphine (e.g. Morphgesic SR /MST Continus).
Divide total daily morphine dose by two and give this dose 12 hourly.
Continue normal release morphine at previous 4 hourly dose but given as hourly prn.

**For patients with severe renal impairment**
- Contact PCT (UHW Ext 43377 UHL Ext 25196 or bleep doctors or nurses via switchboard) /UHW Renal Pharmacy Team (ext 46324 or bleep 5707) for further prescribing advice)
- See Section 4.1.3 for advice on opioid prescribing for patients with severe renal impairment (eGFR < 30mL/min)

**Syringe drivers**
If the patient is nauseated or vomiting, unable to swallow, too weak for oral drugs, unconscious or has poor oral absorption - switch to subcutaneous morphine delivered by syringe driver.

In Cardiff & Vale UHB subcutaneous morphine is used in preference to diamorphine – patients admitted on diamorphine should be converted to morphine with advice from PCT/pharmacy if needed:

Divide 24 hour oral morphine by 2 to give 24 hour SC morphine dose e.g.
60mg oral morphine = 30mg SC morphine = 20mg SC diamorphine
Note: When converting opioid doses, always check with a colleague! Don’t forget to cross off the regular oral opioid once you have prescribed the syringe-driver.

The use of a syringe driver needs to be recorded on the regular drug chart (as “syringe driver-see chart”) and the drugs and doses to be used should be reviewed and prescribed daily on a separate syringe driver chart kept with the main drug chart.

Prescribe 1/6th of syringe driver morphine dose as prn for breakthrough pain.

- If the patient was not previously on a strong opioid give morphine 2.5mg SC stat and then hourly prn. If patient has had full dose codeine (60mg QDS or equivalent) consider using 5mg morphine subcutaneously hourly when required. Commence 24 hour syringe driver when morphine analgesia requirement has been established following 24 hours of prn subcutaneous doses.

- To calculate subsequent 24 hour dose of morphine, total the doses of morphine given over the previous 24 hours (i.e. syringe driver and prn doses) and prescribe the increased syringe driver dose accordingly.

  Top Tip: Further guidance regarding medication for syringe drivers can be found in the Care Priorities document even if the patient is not following these priorities.

iii) Alternative strong opioids

Transdermal (TTS) fentanyl

For a small group of patients the use of TTS fentanyl may be helpful but generally it is not recommended when initially starting a patient on strong opioids. Please contact PCT to discuss if you feel this may be helpful for a patient established on oral morphine who has unacceptable side effects.

Remember that a fentanyl patch is powerful. A 25microgram/hr patch is equivalent to a 24hr dose of oral morphine of 60mg.

Oxycodone (OxyNorm, OxyContin)

Oxycodone is available as a 4-hourly immediate-release preparation (OxyNorm capsules/liquid) and as a 12-hourly sustained release preparation (OxyContin). All patients should be commenced on oral morphine as first line treatment. If however, the patient develops side-effects with morphine (e.g. hallucinations, itching or rash) then switching to oxycodone may be appropriate. (Please also see section 4.1.3 prescribing opioids in severe renal impairment)

NB 10mg oral morphine is equivalent to 5mg oral oxycodone
### iv) Drugs commonly used in a syringe driver (subcutaneous use)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Start dose/24hours (range)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclizine</td>
<td>intestinal obstruction</td>
<td>100-150mg/24hrs</td>
<td>sedative</td>
</tr>
<tr>
<td></td>
<td>nausea unknown cause</td>
<td></td>
<td>skin irritant</td>
</tr>
<tr>
<td>haloperidol</td>
<td>nausea: drug-induced metabolic</td>
<td>1.25-5mg/24hrs</td>
<td>extrapyramidal side effects</td>
</tr>
<tr>
<td></td>
<td>metabolic</td>
<td></td>
<td>rare if low dose</td>
</tr>
<tr>
<td>hyoscine hydrobromide</td>
<td>death rattle, colic, reducing salivation</td>
<td>400 micrograms- 2.4mg/24hrs</td>
<td>antiemetic activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>moderate sedative</td>
</tr>
<tr>
<td>levomepromazine</td>
<td>a. nausea</td>
<td>a. 6.25-25mg/24hrs</td>
<td>skin irritant</td>
</tr>
<tr>
<td></td>
<td>b. sedation for confusion</td>
<td>b. 25-75mg/24hrs</td>
<td>sedative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>useful for agitation in end of life settings</td>
</tr>
<tr>
<td>metoclopramide</td>
<td>impaired gastric emptying e.g. hepatomegaly</td>
<td>30-60mg/24hrs</td>
<td>extrapyramidal side-effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(doses &gt; 30mg should be only used for short periods following palliative care advice)</td>
<td>especially in younger patients use with care in intestinal obstruction</td>
</tr>
<tr>
<td>midazolam</td>
<td>terminal restlessness myoclonic jerking</td>
<td>5-30mg/24hrs</td>
<td>may be used in low dose as an anxiolytic in dyspnoeic or anxious patients</td>
</tr>
<tr>
<td></td>
<td>anticonvulsant</td>
<td>(min 30mg/24hrs for anticonvulsant effect)</td>
<td></td>
</tr>
</tbody>
</table>

Most of the above drugs can be mixed in the same syringe with water for injection but seek advice from pharmacy or PCT if mixing more than 3 drugs.

Common combinations are:
- Morphine + cyclizine (+ haloperidol)
- Morphine + metoclopramide
- Morphine + midazolam + hyoscine
- Morphine + levomepromazine
v) **Constipation**

For opioid-induced constipation

- senna tabs 2 nocte
- senna tabs 2 nocte or 2 bd (or senna liquid 10mL bd – only if patient unable to take tablet) and magnesium hydroxide 10mL od or bd

**or for palliative care patients only**

- co-dantramer 10mL od or bd (can cause skin burns occasionally if faecally incontinent)
- or co-dantramer 1-2 caps od or bd

For resistant constipation with no evidence of intestinal obstruction consider sodium picosulphate or Laxido and ask PCT for further advice.

vi) **Nausea and vomiting**

Identify and treat any causes e.g. constipation, hypercalcaemia, infection.

**Choice of oral antiemetic**

Will depend on most likely cause;

- **drug-induced or metabolic:**
  haloperidol 1.5mg nocte (500 micrograms-1mg in elderly or with severe renal impairment) or cyclizine 50mg tds

- **gastric stasis:**
  suggested by large volume vomitus, early satiety and hiccups
  metoclopramide 10mg tds-qds pre-meals *(doses > 30mg should only be used for short periods following palliative care advice)*

- **cerebral involvement or intestinal obstruction:**
  cyclizine 50mg tds.

Generally antiemetics should be given regularly, not prn, and a combination of the above may be needed. Cyclizine and metoclopramide should not be used together as the anticholinergic effects of cyclizine antagonise the prokinetic effect of metoclopramide. If there is frequent vomiting or severe nausea it may be best to commence a subcutaneous infusion of antiemetics using as appropriate:

- metoclopramide 30-60mg over 24 hours *(doses > 30mg should only be used for short periods following palliative care advice)*
  OR
  cyclizine 150mg over 24 hours
  + / -
  haloperidol 1.25-5mg over 24 hours

  **If problem persists contact PCT.**
vii) Breathlessness, anxiety

- Assess and treat reversible factors e.g. left ventricular failure, infections

Symptomatic management:

- Non-pharmacological management: breathing techniques, activity pacing, anxiety management.
- Facial fan.
- Consider use of oxygen if patient hypoxic; trial of short burst oxygen may be warranted in absence of hypoxia but assessment of benefit undertaken within 72 hours.
- For opioid-naïve patients, in consultation with seniors, consider a trial of a low dose of opioid, even in the absence of pain, to relieve intractable dyspnoea in advanced illness. e.g. oral morphine (Oramorph) 2.5mg or morphine SC 1-2mg prn and titrate upwards with care if benefit described.
- Consider prescribing an anxiolytic if the patient feels panicky with the dyspnoea e.g. lorazepam 0.5-1mg PRN orally up to tds or midazolam 2.5mg SC prn two hourly.

viii) Agitation

- Check for causes such as full bladder or bowels, pain, hypoxia and treat appropriately.
- Prescribe midazolam 2.5mg prn hourly and assess effect. This dose may need to be increased (in approx 50% increments) up to 30mg in 24 hours and a continuous infusion commenced if necessary.

For end of life symptom advice consult Care Priorities document even if the patient is not following these priorities

If symptoms not responding within 24 hours, consult Palliative Care Team for advice

Further advice can be found on [http://book.pallcare.info/](http://book.pallcare.info/)
EMERGENCY TREATMENT OF POISONING

National Poisons Information Service 0844 892 0111

TOXBASE is the primary clinical toxicology database of the National Poisons Information Service and is available to registered users at http://www.toxbase.org/ It provides information about routine diagnosis, treatment and management of patients exposed to drugs, household products, and industrial and agricultural chemicals. It also contains advice on laboratory analytical services, antidote stockholdings and recent toxicological alerts. The regional National Poisons Information Service (Cardiff) is located on Gwenwyn ward, UHL. They may be approached directly or contacted on Ext 25013 for advice on all aspects of poisoning, including access to TOXBASE. Help may also be provided identifying unknown tablets or capsules.

Paracetamol overdose

- Contact the POISONS INFORMATION SERVICE on 0844 892 0111 or check on TOXBASE for the latest management advice of acute and staggered overdoses.
- If the advice is to administer IV acetylcysteine, give in glucose 5% w/v, initial dose 150mg/kg in 200mL over 60 minutes, followed by 50mg/kg in 500mL over four hours, then 100mg/kg in 1L over 16 hours, using the weight-based tables available.

Antidotes

- NALOXONE is used to reverse respiratory depression caused by opioid analgesics.
  
  Note: Analgesia may also be reversed

If the patient has respiratory depression, inadequate airway protection, or has decreased consciousness, give naloxone.

Give an initial dose of 400 micrograms (0.4mg).

- If there is no response after 60 seconds, give a further 800 micrograms (0.8mg).
- If there is still no response after another 60 seconds, give another 800 micrograms (0.8mg).
- If still no response (after a total of 2 mg), give a further 2 mg dose. Large doses (4 mg) may be required in a seriously poisoned patient.
- Aim for reversal of respiratory depression, not full reversal of consciousness.

Once an adequate response has occurred, monitor blood gases, oxygen saturation, and respiratory rate.
IM naloxone is an alternative in the event that IV access is not possible or is delayed. **Failure of a definite opioid overdose to respond to large doses of naloxone suggests that another CNS depressant drug or brain damage is present.**

Observe the patient carefully for recurrence of CNS and respiratory depression. The duration of action of naloxone is shorter than that of all opioid analgesics –

**REPEATED DOSES OF NALOXONE MAY BE REQUIRED.**

**Intravenous infusions following resuscitation**
Intravenous infusions of naloxone are often useful where repeated doses are required. An infusion of 60% of the initial dose required for resuscitation per hour is a useful starting point.

**Infusions are not a substitute for frequent review of the patient's clinical state.**
CHAPTER 1 GASTRO-INTESTINAL SYSTEM

1.1 ‘Nil by mouth’ patients – drug administration

- Patients for investigations e.g. OGD (endoscopy): administer usual medicines with a sip of water – caution with medicines normally requiring a full glass of water for oral administration e.g. alendronic acid (best to delay dose).

- Patients with swallowing difficulties e.g CVA: await assessment.

- Take full drug history in pre-operative assessment – this will identify potential interactions between drugs used during surgery and routine medication.

Pre-operatively

- Some medicine may be taken with up to 300mL of plain tap water only, up until 2 hours before surgery, as clear fluids leave the stomach within 2 hours of ingestion.

- Certain medicines may need to be stopped prior to elective surgery. Specific guidance can be found on the Clinical Portal under Anaesthetics (in Anaesthesia Guidelines and Induction pack).

- Check with anaesthetist if unsure.

Examples

Clopidogrel
The peri-operative management of patients taking clopidogrel depends on the indication for clopidogrel and the degree of bleeding risk anticipated. Refer to the anaesthetist and surgeon for specific advice.

Diuretics
Potassium-sparing diuretics such as spironolactone or amiloride should be omitted on the morning of surgery since tissue damage and reduced kidney perfusion in the immediate post-operative period may predispose to the development of hyperkalaemia.
Do not need to withdraw thiazide or loop diuretics – correct any hypokalaemia before surgery.

Oral hypoglycaemics
Please refer to section on surgery in an individual with diabetes (see Chapter 6 section 6.2).

Warfarin
Refer to the warfarin bridging guidance (on Clinical Portal).
Lithium
Discontinue for 24 hours before any major operation. Provided serum electrolytes are in balance, lithium can and normally should be restarted soon after the operation has been carried out.

**Peri-operatively – where oral route not available**

Consider administering essential drugs by injection, rectally, transdermally, or, if there is no contraindication, via a feeding tube – advice on alternative formulations, bioavailabilities (especially with feeding tubes placed in the jejunum) and equivalent doses can be obtained from your ward pharmacist or Medicines Information on UHW Ext. 42979 or UHL Ext. 25262.

Corticosteroids
Replacement regimen used (usually IV hydrocortisone) to avoid effects of adrenocortical suppression (see BNF).

Anti-Parkinsonian drugs
Always give usual anti-parkinsonian medications before surgery. Dispersible tablets and/or liquids are available for some drugs. Contact your ward pharmacist or Parkinson’s Disease Nurse for further advice.

### 1.2 Acid suppression therapy

*Note: Omeprazole and lansoprazole are currently the proton pump inhibitors (PPIs) in the UHB formulary. Generic omeprazole is currently the cheapest PPI available.*

- Omeprazole can occasionally potentiate the effects of phenytoin and warfarin (monitor INR).
- If initiating a patient on a PPI then please state on the Discharge Advice Letter (DAL), the indication, duration of required treatment and if, or when, step-down treatment should be considered.

Gastrooesophageal reflux disease (GORD)
*NICE CG 184 – Dyspepsia and gastro-oesophageal reflux disease, September 2014*

- stepped approach:
  - Initially life style advice (stopping smoking, low fat diet, weight loss if obese and raising the head of the bed [using 3 bricks] for nocturnal symptoms) plus
  - Simple antacids e.g. magnesium trisilicate.
  - Gaviscon Advance, 5-10mL after meals and at bedtime or Gastrocote, a low sodium alternative (1.8mmol Na⁺/5mL), are rafting antacids.
  - If ineffective switch to omeprazole 20mg daily or lansoprazole 30mg od.
  - Recommend a 4-week course of full dose PPI for new onset symptoms. If symptoms recur, continue at the lowest dose that controls symptoms e.g. omeprazole 10mg od, lansoprazole 15mg od.
  - Ranitidine 150mg bd is an option if intolerant to PPIs e.g. severe diarrhoea or for
milder symptoms (as treatment or maintenance).

- See section 1.15.3 for new guidance on domperidone.

Severe GORD symptoms or oesophagitis

- Offer a full dose PPI (omeprazole 20mg or lansoprazole 30mg daily) for 8 weeks.
- The maintenance dosage should be that which gives symptomatic relief. Some patients will require omeprazole 20-40mg or lansoprazole 30mg daily to achieve this.
- Higher doses may be required if endoscopically proven oesophagitis fails to heal.
- For those who have required dilation of a peptic oesophageal stricture or have Barretts Oesophagus, long term maintenance with omeprazole 20mg or lansoprazole 30mg is recommended.

Non-ulcer dyspepsia (Functional dyspepsia)

- If H. pylori present, consider eradication therapy (see below).
- If H. pylori excluded and symptoms persist, offer either a low dose PPI or H₂ antagonist (e.g. ranitidine) for 4 weeks.
- If symptoms continue or recur after initial treatment offer a PPI or H₂ antagonist at lowest dose to control symptoms.

1.3 Peptic ulceration

1.3.1 H. pylori related ulcers:

- Treat with triple therapy for one week using:
  - omeprazole 20mg bd or lansoprazole 30mg bd
  - amoxicillin 1g bd
  - metronidazole 400mg bd or clarithromycin 500mg bd
  (if patient has penicillin allergy change amoxicillin to clarithromycin 500mg bd or if patient has an intolerance to metronidazole change metronidazole to clarithromycin).

For extensive ulceration complicated by haemorrhage or perforation continue omeprazole 20mg or lansoprazole 30mg daily for four weeks only.

Note: All gastric ulcers should have follow up gastroscopy with biopsies until healed, initially at 6 weeks. For duodenal ulcers follow up endoscopy is not indicated if asymptomatic.

1.3.2 Non-steroidal anti-inflammatory drug (NSAID)-related ulcers:

- Treat with omeprazole 20mg or lansoprazole 30mg daily for 8 weeks and stop NSAID if at all possible.

- For patients with a NSAID-induced ulcer who need to continue NSAID treatment, a PPI should continue to be co-prescribed.

- NSAIDs should be taken with food and used at the lowest effective dose for the shortest duration necessary.
  - First choice: ibuprofen
  - Second choice: naproxen
  - Not recommended: azapropazone
If *H. pylori* positive prescribe triple therapy (see above) in both NSAID and aspirin related bleeds, and give PPI prophylaxis if aspirin or NSAID continued.

Selective serotonin re-uptake inhibitors (SSRIs) should be used with caution in patients who have an increased risk of gastrointestinal bleeding, especially in patients taking NSAIDs or aspirin. A non-SSRI antidepressant may be an appropriate choice in such patients.

Oral anticoagulants or corticosteroids should be used with caution in patients at risk from gastrointestinal bleeding especially in those taking aspirin or NSAIDs.

Consider prophylaxis of NSAID-related ulceration with lansoprazole or omeprazole for patients with high risk factors e.g. elderly, history of peptic ulcer, other underlying disease, concomitant steroids.

Selective Cox 2 inhibitors (e.g. celecoxib) should not routinely be used. They should only be used for patients who are at a particularly high risk of developing gastroduodenal ulcer, perforation or bleeding AND after an assessment of cardiovascular risk. Selective Cox 2 inhibitors and diclofenac should not be used in patients who have ischaemic heart disease, cerebrovascular disease, peripheral arterial disease or congestive heart failure.

If NSAID-related ulcer suspected, please complete a yellow adverse drug reaction reporting form.

### 1.4 Acute upper gastrointestinal haemorrhage

- Assess risk using Blatchford score (at presentation) and Rockall score (after gastroscopy)
- Keep patient nil by mouth until endoscoped (should be next day, or as emergency if severe bleeding)
- If platelets below 50 and active bleeding, give platelet transfusion.
- If fibrinogen below 1 g/L, or PT or APTT >1.5 normal, and active bleeding, give fresh frozen plasma.

**Acid suppression therapy**

- PPIs are indicated if an ulcer is strongly suspected. Only use IV bolus omeprazole in patients who cannot physically swallow an oral PPI.
- Treat peptic ulceration (see section 1.3)

**IV omeprazole following endoscopic haemostasis of bleeding peptic ulcers**

- After therapeutic treatment for bleeding ulcer (if recommended by endoscopist), give IV omeprazole 80mg bolus followed by a continuous infusion of 8mg/hour for 72 hours (ie 40mg omeprazole in 100mL sodium chloride 0.9% or glucose 5% w/v over 5 hours – then set up another infusion).
- Initiate oral PPI therapy after 72 hours for a minimum of 4 weeks e.g. omeprazole 20mg od or lansoprazole 30mg od.
Anticoagulants and antiplatelet drugs in acute GI bleeding

- Offer prothrombin complex concentrate to patients who are taking warfarin and are actively bleeding.

- Discuss the management of patients on treatment doses of the new oral anticoagulants (apixaban, dabigatran, rivaroxaban) with the haematologist on call.

- Stop aspirin at initial assessment, but if haemostasis is achieved: aspirin may be restarted.

- Stop clopidogrel, prasugrel, ticagrelor and dipyridamole at initial assessment, but discuss risk/benefits of continuing with cardiologist/haematologist once bleeding controlled.

- Stop apixaban, dabigatran, rivaroxaban at initial assessment but discuss risks/benefits of continuing with cardiologist/haematologist once bleeding is controlled.

1.5 Terlipressin for oesophageal varices

- If oesophageal varices known or strongly suspected use terlipressin 2mg IV bolus every 4-6 hours for up to 72 hours.

  *Note: In patients with angina or known coronary artery disease a GTN patch 10mg should be applied ONCE DAILY whilst the patient is receiving terlipressin*

1.6 Use of PPIs in patients nil by mouth

- Do not use IV PPIs for treatment of reflux oesophagitis or peptic ulcers in patients nil by mouth. IV PPIs should only be used if recommended by the duty endoscopist.

- Use PPIs via NG tube wherever possible e.g. lansoprazole orodispersible tablets.

- Patients “nil by mouth” prior to surgery – consider oral PPI.

- Patients “nil by mouth” post-op – consider oral PPI or ranitidine 50mg IV tds.

- For prophylaxis of stress ulceration – consider sucralfate.

1.7 Management of hepatic encephalopathy

grade 1  mild confusion  
grade 2  drowsy, gross mental ability defects  
grade 3  somnolent, rousable, speech incomprehensible  
grade 4  coma

Seek precipitating cause including GI bleed, sepsis, abnormal electrolytes, or drugs (e.g. sedative use).
Assessment: All jaundiced patients should complete 5-pointed star and document hand-writing on admission. This should be repeated daily to monitor degree of encephalopathy.

Treatment: lactulose oral or via NG tube. Increase dose until 2-3 loose stools per day. If unable to give by oral route, use lactulose washouts PR daily (300mL made up to 1L in water). All jaundiced patients should receive normal protein diet i.e. 1g/kg body weight. Do not restrict protein intake unless failure to respond to aggressive treatment. Consider therapeutic trial of flumazenil if recent benzodiazepines, e.g. for gastroscopy.

1.8 Laxatives

- **Identify and where possible correct cause** of constipation, consider:
  - Underlying disease
  - Decreased mobility
  - Change in diet
  - Pregnancy
  - Dehydration
  - Mechanical obstruction - confirmed faecal mass by PR
  - Drugs - opiates, anticholinergics, calcium channel blockers, iron

- **Educate patient**: mobilise where possible; refer to dietician for increased fluid and fibre intake.

- **Acute constipation** (suitable for short term use)
  a. Senna tabs 2 nocte prn.
  b. Glycerin 4g supp 1 daily prn.
  c. Micro-enema 1 daily prn.
  d. Phosphates Enema 1 daily prn.
  *For impaction use Micro-enema at night to soften stool then Phosphates Enema next morning.*

- **Chronic constipation** (suitable for long term use)
  a. Isphaghula husk sachets (e.g. Fybogel) 1 bd
  b. Senna tabs 2 nocte 2x a week

**Long term use of senna is not recommended in younger people.**

**Opiate-induced constipation**

a. Senna tabs 2 nocte
b. Senna tabs 2 nocte or 2 bd (or Senna liquid 10mL nocte or 10mL bd if patient unable to swallow tablets) + magnesium hydroxide 10mL bd *

- Co-danthramer strong suspension or capsules†

* The cost of senn/magnesium hydroxide liquids is 15 times that of senna tablets and are suggested second line
† expensive – should not be used first line; co-danthramer and co-danthrusate are only licensed for constipation in terminally ill patients of all ages (avoid in patients with faecal incontinence)
LACTULOSE is not recommended in the routine management of constipation. It has limited efficacy in acute constipation, is unpalatable to some patients and its’ daily cost is 20 times that of senna tablets. It may be used to prevent hepatic encephalopathy in a dose of 30mL tds, adjusted to produce 2-3 soft stools daily.

1.9 Bowel preparation
- Clear fluids only from day before procedure and nil by mouth on the day of procedure.
- Klean-Prep – 2 sachets in 2 litres of water during the afternoon and 2 sachets in 2 litres of water during the evening of day before procedure. If patient on afternoon list, 2 sachets in 2 litres of water during the evening before the procedure and 2 sachets in 2 litres of water during the morning of the day of the procedure. Give metoclopramide 10mg IM or IV (over 2 minutes) if the patient develops nausea and vomiting.
- Moviprep – morning procedure: 2 sachets in one litre of water during afternoon before, and 2 sachets in one litre of water in early evening. If patient on afternoon list, 2 sachets in one litre during the evening before the procedure and 2 sachets in one litre during the morning of the day of the procedure. Patient should continue to drink plenty of water or clear fluids (at least 500mL extra with each litre of Moviprep).
- Inpatients: if necessary add Phosphates Enema on the morning of procedure.

1.10 Octreotide for enterocutaneous or pancreatic fistulae
(Unlicensed indications)
- Warm vials to room temperature prior to injection to reduce pain and irritation.
- Commence treatment with a small dose, i.e. 50 micrograms SC bd.
- Monitor and document beneficial and adverse effects.
- Dose may need to be increased to 200 micrograms SC tds to achieve maximal response.
- Benefit should be seen within 48 hours. Consider withdrawing octreotide if response is poor at the maximum dose.
- Stop octreotide when fistula closed.
- Depot preparations of octreotide are available as 10mg, 20mg and 30mg vials for longer term use.

1.11 Administration of drugs through a gastrostomy/ jejunostomy tube
For administration of drugs via a gastrostomy/jejunostomy tube contact ward pharmacist or Medicines Information on UHW Ext 42979 or UHL Ext 25262.

1.12 Use of pancreatic enzymes to unblock feeding tubes
(Unlicensed indication)
1. Open a Creon 10000 capsule (or equivalent) and dissolve contents of capsule in 5-10mL sodium bicarbonate 8.4%.
2. Instil the solution into the feeding tube.
3. After 5 minutes, flush feeding tube with 30mL water.
1.13 Severe acute colitis

- Start IV hydrocortisone 100mg qds and Predsol enemas one bd.
- Enoxaparin prophylaxis 40mg SC od (due to increased thrombotic risk) unless contraindicated.
- Stool cultures to exclude infection. Test for C.difficile.
- Abdominal x-ray to exclude toxic megacolon.
- Check ESR, CRP, FBC and LFTs.
- Refer to Gastroenterology team as soon as possible for continuing treatment and liaison with GI surgeons.

1.14 Omnipaques for in-patient CT scanning

- Omnipaques 350 is a specially formulated non-ionic gastro-intestinal contrast agent that is used to opacify bowel prior to CT. It is diluted in water and taken over a period of time to ensure that, in particular, the small bowel is opacified in order to optimise image interpretation. If colonic pathology is suspected, a longer period of preparation is required.

- Omnipaques 350 can be taken orally or given via an NG tube. Patients who are unable to swallow, or at risk of aspiration, must be given Omnipaques via the NG route. If aspirated, Omnipaques can cause a chemical pneumonitis.

- Contraindications include hypersensitivity to iodine-containing contrast media and manifest hyperthyroidism.

- Omnipaques 350 must be prescribed before being given. Prescribe on the ‘stat’ side of the chart as “Omnipaques 350 prior to CT scan”, “Dose – as per CT protocol”.

Usual instructions and timings in relation to CT scan are as below:

- **Abdomen & Pelvis CT scans (including pancreatitis follow-up)**
  20mL of Omnipaques 350 diluted to 500mL with water or squash.
  250mL of this should be taken 60 minutes before the scan, and the remaining 250mL should be taken 30 minutes before the scan.

- **Minimal preparation CT scans** – requires prolonged oral preparation from 24 hours before the scan to opacify the colon.

  **On the day before the scan:**
  25mL of Omnipaques 350 to be diluted to 500mL with water or squash.
  250mL to be taken 24 hours before the scan, and the other 250mL to be taken 12 hours before the scan.

  **On the day of the scan:**
  25mL of Omnipaques 350 to be diluted to 500mL with water or squash.
  250mL to be taken 60 minutes before the scan and the other 250mL to be taken 30 minutes before the scan.
Extended preparation - Occasionally a 2 hour preparation is required
50mL of Omnipaque 350 to be diluted to 1 litre with water or squash.
500mL to be taken 2 hours before the scan,
250mL 1 hour before the scan,
250mL 30 minutes before the scan.

Further Omnipaque 350 or water will be given to the patient in the department
before any scan if required.

For further advice contact Radiology on UHW Ext 45557 or UHL Ext 25279

1.15 Anti-emetics

1.15.1 Ondansetron
Drug Safety Update, August 2012

- Ondansetron should be avoided in patients with congenital long QT syndrome.

- Use with caution in patients with risk factors for QT interval prolongation or
cardiac arrhythmias, e.g. electrolyte abnormalities, use of medicines that prolong
QT interval (including cytotoxic drugs) or that may lead to electrolyte
abnormalities, congestive heart failure, bradyarrhythmias or use of medicines
that lower heart rate.

- Hypokalaemia and hypomagnesaemia should be corrected before
ondansetron administration.

1.15.2 Metoclopramide
Drug Safety Update, August 2013

- Metoclopramide is indicated for postoperative nausea and vomiting, radiotherapy-
induced nausea and vomiting, delayed (but not acute) chemotherapy-induced
nausea and vomiting, and symptomatic treatment of nausea and vomiting,
including that associated with acute migraine.

- Intravenous doses should be administered as a slow bolus over at least
3 minutes to reduce the risk of adverse effects.

- In order to minimise the risk of potentially serious neurological adverse effects
  - metoclopramide should only be prescribed for short-term use (up to 5 days)
  - For adults, the maximum dose in 24 hours is 30mg (or 0.5mg per kg
    bodyweight). The usual dose is 10mg up to three times a day.

1.15.3 Domperidone
Drug Safety Update, May 2014

- Domperidone is associated with a small increased risk of serious cardiac side
effects.
• Its use is now restricted to the relief of nausea and vomiting and the dosage and duration of use have been reduced. It should no longer be used for the treatment of bloating and heartburn.
• Domperidone is now contraindicated in people:
  - with conditions where cardiac conduction is, or could be, impaired
  - with underlying cardiac disease such as congestive heart failure
  - receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors
  - with severe hepatic impairment
• Patients with these conditions and patients receiving long-term treatment with domperidone should be reassessed at a routine appointment, in light of the new advice.
• For adults and adolescents over 12 years of age and weighing 35kg or more, the recommended maximum oral dose in 24 hours is 30mg (dose interval: 10mg up to three times a day)
• Suppositories should only be used in adults and adolescents weighing 35kg or more, the recommended maximum daily dose in 24 hours is 60mg (dose interval: 30 mg twice a day).
• The maximum treatment duration should not usually exceed one week.
1.16 Guidelines for Postoperative Nausea & Vomiting (PONV)

Cardiff and Vale NHS Trust Directorate of Anaesthetics
Guidelines for Postoperative Nausea & Vomiting (PONV)

Prophylaxis of PONV in adults

**Basic Risk Factors**
- Obesity
- Female gender
- Non smoker
- History of migraine
- Oral surgery
- ENT surgery

**High Risk Factors**
- History of PONV
- History of motion sickness
- Squint surgery
- Gynae surgery
- Laparoscopic surgery

Patients at risk of PONV
(1 basic risk factor)

Follow treatment flow-chart if PONV occurs

Patients at high risk of PONV
(1 high risk factor or >1 basic risk factor)

Prescribe IV ondansetron 4mg
(intraoperatively*)

Patients at very high risk of PONV
(>1 high risk factor)

Prescribe IV ondansetron 4mg
Plus
IV dexamethasone 8mg
(intraoperatively*)

*consider prescribing the same dose orally as pre-medication on ward
Treatment of PONV in adults

Patient nauseous/vomiting

Consider likely causes(s)/exacerbating factors* and treat where possible

Has cyclizine been administered in the last 4 hrs?

Yes

Give prochlorperazine 3mg buccal or 12.5mg IM stat

** Ineffective

Give ondansetron 4mg slow IV stat

Effective

Prescribe regular Buccastem (max 3-6mg bd)

Has < 150mg cyclizine been administered in the last 24 hrs?

No

Give cyclizine 50mg IV/IM stat

** Ineffective

Give cyclizine 50mg IV/IM stat

** Ineffective

Refer to Acute Pain Service

Effective

Prescribe cyclizine PO/IM (max:50mg tds)

* Potential causes of nausea: dehydration, low/high blood glucose, U&E imbalance, morphine sensitivity (contact Acute Pain Service), antibiotic/drug therapy, pain, anxiety, hypoxia, ileus, hypotension

** Please allow a minimum of 1 hour to establish treatment failure.

Regular assessment of treatment is essential.

N.B PONV should only affect the patient for around 72 hours post op.
## 1.17 Mesalazine prescribing guidance: mild to moderate Ulcerative Colitis

The most cost effective mesalazine preparation should be chosen. Issues of compliance and tablet burden may occasionally impact. There is a lack of proven clinical superiority between brands.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Acute</th>
<th>Maintenance</th>
<th>Cost (8 weeks treatment) acc to BNF No.66</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORAL TREATMENT</strong></td>
<td></td>
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<tr>
<td>If able to use granules:</td>
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<tr>
<td>Salofalk granules: 1.5 and 3g sachets</td>
<td>3g OD (1 x 3g sachet)</td>
<td>1.5g-3g sachet OD</td>
<td>3g £91 1.5g £46</td>
</tr>
<tr>
<td>Salofalk 500mg tablets or Pentasa 1g tablets</td>
<td>3g OD (6 Salofalk tablets) 4g OD (4 Pentasa tablets)</td>
<td>1.5-3g OD (3-6 Salofalk tablets OD) 2-4g OD (2-4 Pentasa tablets OD)</td>
<td>3g Salofalk £109 1.5g Salofalk £54 4g Pentasa £138 2g Pentasa £69</td>
</tr>
<tr>
<td>Asacol 800mg tablets or Mezavant 1.2g tablets</td>
<td>2.4g OD (3 Asacol tablets) 2.4g OD (2 Mezavant tablets)</td>
<td>2.4g OD</td>
<td>2.4g Asacol £110 2.4g Mezavant £117</td>
</tr>
<tr>
<td><strong>RECTAL TREATMENT</strong></td>
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<tr>
<td>(4 weeks treatment at commonly used dose – BNF No 66.)</td>
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<tr>
<td>See INFORM for approved rectal steroid treatments – prednisolone and budesonide</td>
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<tr>
<td><strong>Enema therapy</strong></td>
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</tr>
<tr>
<td>1g Asacol foam £108 1g Salofalk foam £121 1g Pentasa liquid £71</td>
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<td></td>
</tr>
<tr>
<td><strong>Suppository therapy</strong></td>
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</tr>
<tr>
<td>(Use in proctitis +/- oral therapy)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1g Salofalk £56 1g Pentasa £40</td>
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</tr>
</tbody>
</table>
1) Addition of enemas to oral therapy gives additional benefit, both in left-sided and extensive disease, with best evidence for Pentasa oral and enema

2) No evidence that 4.8g Asacol is better than 2.4g for mild acute UC; for moderate acute UC there is some evidence that symptom resolution is slightly faster. No evidence of benefit for 4.8g Mezavant over 2.4g in mild or moderate acute UC. Consider higher doses in patients who flare on 2.4g maintenance.

3) After 8 weeks consider reducing dose for patients in complete clinical remission. Some advise continuing induction dose for one year, and generally relapse risk increases as dose is lowered.

4) Mesalazine enemas are more effective than steroid enemas in most analyses. Most patients tolerate foam enemas better than liquid, although liquid can be inserted gently, and foam is by metered dose at fixed pressure.
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 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 after excluding brain haemorrhage. 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 – after an acute stroke (both ischaemic and haemorrhagic strokes) blood pressure should be reduced to around 140/80mmHg as soon as possible and maintained at that level. The frequency of blood pressure measurement should be tailored to individual needs of acute stroke patients. (Please refer to INTERACT2 and ENOS trials: Lower BP improves outcomes and the benefit is time dependent occurring mostly in the first 6 hours).

- 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 (26–48mmol/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 a 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 bendroflumethiazide (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</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 >85kg
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 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.
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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.
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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 intracardiac 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.

- 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
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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 management 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 an 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.
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\textsubscript{1C} agents e.g. flecainide, propafenone</td>
<td>None</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>Sotalol, Amiodarone, Dronedarone</td>
<td>All Class\textsubscript{1C} absolutely contraindicated</td>
</tr>
<tr>
<td>Hypertension/Hypertrophy</td>
<td>Class\textsubscript{1C}, Amiodarone, Dronedarone</td>
<td>Sotalol</td>
</tr>
<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 contraindicated 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 $\equiv$ 625 micrograms po).
**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)
  [http://www.cardiffandvale.wales.nhs.uk/pls/portal/url/ITEM/1ED0904CE2FF5D9DE0500489923C09E8](http://www.cardiffandvale.wales.nhs.uk/pls/portal/url/ITEM/1ED0904CE2FF5D9DE0500489923C09E8)

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).
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 ≥180mmHg or diastolic BP ≥110mmHg and offer antihypertensive treatment to patients where BP is ≥160/100mmHg.
- 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 ≥20%.
- For patients aged less than 80 years a target clinic BP of lower than 140/90mmHg is recommended. For patients aged over 80 years a target clinic BP of lower than 150/90mmHg is recommended.
- For patients with Type 2 diabetes the BP target is <140/80mmHg (<130/80mmHg 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.
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)

Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients

**Resistant hypertension**
A or ARB + C + D + consider diuretic or alpha- or beta-blocker.
(spirotolactone 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

Call Resuscitation Team

CPR 30:2
Attach defibrillator / monitor
Minimise interruptions

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

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

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

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
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, SpO₂, record 12-lead ECG
- Identify and treat reversible causes (e.g. electrolyte abnormalities)

**Synchronised DC Shock**
Up to 3 attempts

- Amiodarone 300mg IV over 10-20 min and repeat shock; followed by:
- Amiodarone 900mg over 24 hours

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

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

- **NARROW**
  - Regular
    - 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

- **BROAD**
  - Irregular
    - Seek expert help
      - Possibilities include:
        - **AF with bundle branch block**
          treat as for narrow complex
        - **Pre-excited AF**
          consider amiodarone
        - **Polymorphic VT** (e.g. torsade de pointes – give magnesium 2g over 10 min)

- **Yes/Unstable**
  - **Synchronised DC Shock**
  - Up to 3 attempts

- **No/Stable**
  - **Is QRS narrow (< 0.12 sec)?**
  - **BROAD**
  - Irregular
    - Seek expert help
      - Possibilities include:
        - **AF with bundle branch block**
          treat as for narrow complex
        - **Pre-excited AF**
          consider amiodarone
        - **Polymorphic VT** (e.g. torsade de pointes – give magnesium 2g over 10 min)
Cardiovascular System

NARROW

Regular

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

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

Irregular Narrow Complex Tachycardia

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

Irregular

Is rhythm regular?

Seek expert help

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

**Seek expert help**
Arrange transvenous pacing

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

**Observe**

* 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 (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 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.

* note maximum dose of simvastatin is 20mg daily with concomitant amiodarone, verapamil, diltiazem or amlodipine 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)

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 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 2.3-4.5mmol/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 unacceptable side-effects have occurred, **decrease to 2mL/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 3mL/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**

* 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.

**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.
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:**
- 18 years 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
Exclusion Criteria (refer directly to on-call medical team)
- < 18 years 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 or 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>Cellulitis</th>
<th>Torn gastrocnemius (calf) muscle</th>
</tr>
</thead>
<tbody>
<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>
**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>Long-term</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:
- if D-dimers are raised one month after discontinuing anticoagulation
- presence of antiphospholipid antibodies
- in a male
- 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).
Cardiovascular System

- 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
- All patients should have a
  - 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](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 LMWH 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.
- 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>Day 8</td>
<td>(This INR is predictive of maintenance dose in the majority of patients)</td>
</tr>
<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
Cardiovascular System

(outpatients or new admissions) or Adult Inpatient Warfarin Treatment Chart.

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

<table>
<thead>
<tr>
<th>MAINTENANCE dosing for all patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing guidelines for patients who have been taking warfarin for 7 days or longer</td>
</tr>
<tr>
<td>Target INR</td>
</tr>
<tr>
<td>2.5</td>
</tr>
<tr>
<td>3.5</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)
- Newly diagnosed DVT (Acute Response Team)

The patient’s INR monitoring must be confirmed by one of these services prior to
Cardiovascular System

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://nww.cardiffandvale.wales.nhs.uk/pls/portal/docs/PAGE/CARDIFF_AND_VALE_INTRANET/TRUST_SERVICES_INDEX/PHARMACY_CP/OUTPATIENTS_REFERRALS/INR%20CLINIC%20REFERRAL%20220212.PPT](http://nww.cardiffandvale.wales.nhs.uk/pls/portal/docs/PAGE/CARDIFF_AND_VALE_INTRANET/TRUST_SERVICES_INDEX/PHARMACY_CP/OUTPATIENTS_REFERRALS/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.
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:

<table>
<thead>
<tr>
<th>DATE &amp; START</th>
<th>INFUSION FLUID</th>
<th>ROUTE</th>
<th>MEDICINE ADDED</th>
<th>INFUSION RATE</th>
<th>SIGNATURE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TYPE/ STRENGTH</td>
<td>VOLUME</td>
<td>APPROVED NAME</td>
<td>DOSE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal Saline</td>
<td>20 mL</td>
<td>Heparin</td>
<td>20,000 units</td>
<td>As per heparin chart</td>
</tr>
</tbody>
</table>

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</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</td>
</tr>
<tr>
<td></td>
<td>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 ≥50% from that recorded immediately before commencing heparin therapy, occurring ≥5 days (and usually <10 days) after initial heparin exposure.

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

NOTES
- In surgical patients a fall in platelets by ≥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 <5 days.
- Severe thrombocytopenia (<15 x 10⁹/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 x 10⁹/L</td>
<td>30-50% fall or platelet nadir 10-19 x 10⁹/L</td>
<td>Fall &lt;30% or platelet nadir &lt;10 x 10⁹/L</td>
</tr>
<tr>
<td><strong>Timing of platelet fall or other sequelae</strong></td>
<td>Clear onset between days 5-10 Or ≤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 ≤1d if heparin 30-100d ago</td>
<td>Platelet count fall ≤4 days without recent heparin exposure)</td>
</tr>
<tr>
<td><strong>Thrombosis or other skin sequelae</strong></td>
<td>• New thrombosis • Skin necrosis • Post-heparin bolus acute systemic reaction</td>
<td>• Progressive or recurrent thrombosis • erythematous skin lesions • suspected thrombosis</td>
<td>None</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

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

Score ≥4

Stop heparin

Start argatroban

Notes

- 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.

ON-GOING MANAGEMENT

- 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:

<table>
<thead>
<tr>
<th>DATE &amp; START</th>
<th>INFUSION FLUID TYPE/STRENGTH</th>
<th>VOLUME</th>
<th>ROUTE</th>
<th>MEDICINE ADDED</th>
<th>DOSE</th>
<th>INFUSION RATE</th>
<th>SIGNATURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Todays date</td>
<td>Sodium Chloride 0.9% or Glucose 5%</td>
<td>250 mL</td>
<td>i.v.</td>
<td>Argatroban</td>
<td>250mg</td>
<td>As per argatroban chart</td>
<td>Doctor signature</td>
</tr>
</tbody>
</table>

- 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:-

<table>
<thead>
<tr>
<th>Body Weight (kg)</th>
<th>Infusion rate (mL/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Liver Impairment / post cardiac surgery / critically ill</em></td>
<td>All other patients</td>
</tr>
<tr>
<td>0.5 micrograms/kg/min</td>
<td>2 micrograms /kg/min</td>
</tr>
<tr>
<td>50</td>
<td>1.5</td>
</tr>
<tr>
<td>60</td>
<td>1.8</td>
</tr>
<tr>
<td>70</td>
<td>2.1</td>
</tr>
<tr>
<td>80</td>
<td>2.4</td>
</tr>
<tr>
<td>90</td>
<td>2.7</td>
</tr>
<tr>
<td>100</td>
<td>3.0</td>
</tr>
<tr>
<td>110</td>
<td>3.3</td>
</tr>
<tr>
<td>120</td>
<td>3.6</td>
</tr>
<tr>
<td>130</td>
<td>3.9</td>
</tr>
<tr>
<td>140</td>
<td>4.2</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>APTT (s)</th>
<th>Infusion Change</th>
<th>APTT (s)</th>
<th>Infusion change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5</td>
<td>Increase by 0.1 micrograms/kg/min</td>
<td>&lt;1.5</td>
<td>Increase by 0.5 micrograms/kg/min</td>
</tr>
<tr>
<td>1.5 – 3.0</td>
<td>No change</td>
<td>1.5 – 3.0</td>
<td>No change</td>
</tr>
<tr>
<td>&gt;3.0</td>
<td><strong>STOP</strong> until &lt;3.0. Restart at half previous rate</td>
<td>&gt;3.0</td>
<td><strong>STOP</strong> until &lt;3.0. Restart at half previous rate</td>
</tr>
</tbody>
</table>
Cardiovascular System

- 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. If 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.

**Box 1 Risk factors for VTE**

- Active cancer or cancer treatment
- Age over 60 years
- Critical care admission
- Dehydration
- Known thrombophilias
- Obesity (body mass index (BMI) over 30 kg/m²)
- One or more significant medical co morbidities (for example: heart disease; metabolic, endocrine or respiratory pathologies; acute infectious disease; inflammatory conditions)
- Personal history or first-degree relative with a history of VTE
- Use of hormone replacement therapy
- Use of oestrogen-containing contraceptive therapy
- Varicose veins with phlebitis
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).
CHAPTER 3 RESPIRATORY SYSTEM

3.1 Inhaler therapy

Many inhalers are available and each has differing properties. Often metered dose inhalers (MDIs) will provide an effective option. However, patients’ age, attitude, physical ability, breathing and co-ordination may influence choice. Also device characteristics such as ease of use, ease of teaching technique, compatibility with other devices, inspiratory flow rate required, available strengths and cost should be considered before prescribing.

Inhaler devices

1) Metered Dose Inhaler (MDI) A hand operated device requiring dexterity and co-ordination. Inhaler technique is critical for effective dosing.

<table>
<thead>
<tr>
<th>Short acting beta₂-agonist</th>
<th>Salbutamol</th>
<th>100-200 micrograms prn/qds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting beta₂-agonist (LABA)</td>
<td>Salmeterol</td>
<td>50 micrograms bd</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Ipratropium</td>
<td>40 micrograms qds</td>
</tr>
<tr>
<td>Steroid</td>
<td>Beclometasone#</td>
<td>100-500 micrograms bd*</td>
</tr>
<tr>
<td></td>
<td>Fluticasone</td>
<td>50-250 micrograms bd*</td>
</tr>
<tr>
<td>Combination</td>
<td>Seretide (fluticasone &amp; salmeterol)</td>
<td>various strengths</td>
</tr>
<tr>
<td></td>
<td>Fostair (beclometasone &amp; formoterol)</td>
<td>100/6 micrograms 1-2 puffs bd</td>
</tr>
</tbody>
</table>

NB Qvar 50 micrograms is equivalent to Clenil Modulite 100 micrograms.
# Beclometasone MDIs must be prescribed by brand name as they are not dose equivalent.
* The above are examples of usual dose ranges, higher doses may be used in some patients.

When changing to Qvar from Clenil if (a) control is good on Clenil change to Qvar at half the dose; (b) control is not good on Clenil change to Qvar at the same dose.

Spacer devices are designed to ease the use of MDIs. Less co-ordination is needed for use. They may improve efficacy and reduce adverse effects (especially when using inhaled corticosteroids) although patients still need education in their use. The device compatible with the MDI should be chosen and maintenance advice given.

N.B. arthritic patients – consider “Haleraid” device.

Some metered dose inhalers exist in a breath-actuated form, the drug being automatically released as the patient inhales. They need to be primed before use.
e.g. “Easi-Breathe” range (salbutamol, beclometasone) “Autohaler” (salbutamol, beclometasone)

2) Dry Powder Devices Dry powder devices require a steady inhalation to deliver the dose satisfactorily to the lower airways.
Respiratory System

a) **Turbohaler** Requires a strong and relatively fast inhalation. Suitable for patients with poor co-ordination though a certain amount of dexterity is still needed. Attachments exist for arthritic patients (turbohaler grip).

<table>
<thead>
<tr>
<th>Type</th>
<th>Drug(s)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist</td>
<td>Terbutaline</td>
<td>500 micrograms prn/4-6 hourly</td>
</tr>
<tr>
<td>Long-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist</td>
<td>Formoterol</td>
<td>6-12 micrograms od-bd increasing to 24 micrograms bd. Maximum short term dose 72 micrograms daily</td>
</tr>
<tr>
<td>Steroid</td>
<td>Budesonide</td>
<td>100-800 micrograms bd</td>
</tr>
<tr>
<td>Combination</td>
<td>Symbicort (budesonide &amp; formoterol)</td>
<td>various strengths</td>
</tr>
</tbody>
</table>

**NB** Usual licensed dose of Accuhaler is ONE puff bd – caution as most other inhaled products (e.g. MDIs) require two puffs to give the necessary dose.

b) **Accuhaler** Requires a steady and strong inhalation. Some dexterity and technique still needed.

<table>
<thead>
<tr>
<th>Type</th>
<th>Drug(s)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist</td>
<td>Salbutamol</td>
<td>200-400 micrograms prn/qds</td>
</tr>
<tr>
<td>Long-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist</td>
<td>Salmeterol</td>
<td>50-100 micrograms bd</td>
</tr>
<tr>
<td>Steroid</td>
<td>Fluticasone</td>
<td>100-500 micrograms bd</td>
</tr>
<tr>
<td>Combination</td>
<td>Seretide (fluticasone &amp; salmeterol)</td>
<td>various strengths</td>
</tr>
</tbody>
</table>

c) **Easyhaler** Requires a strong and relatively fast inhalation

<table>
<thead>
<tr>
<th>Type</th>
<th>Drug(s)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist</td>
<td>Salbutamol</td>
<td>100-200 micrograms prn/qds</td>
</tr>
<tr>
<td>Long-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist</td>
<td>Formoterol</td>
<td>12-24 micrograms bd</td>
</tr>
<tr>
<td>Steroid</td>
<td>Budesonide</td>
<td>100-800 micrograms bd</td>
</tr>
</tbody>
</table>

If advice is required on any aspect of inhaler therapy please contact your ward pharmacist. Inhaler technique must be checked regularly and not presumed to be correct. Full details on suggested inhaler choices can be found on the **GP Referral & Pathway Guidance** section of the intranet under the Asthma, COPD & Oxygen heading.

### 3.2 Nebulised therapy

Ensure appropriate carrier gas used

**Either**

1. **Oxygen** - In acute asthma (stating flow rate and concentration – a flow rate of at least 8L/minute using a medium concentration mask will give approximately 60% oxygen) or Type I respiratory failure (normal/low PaCO<sub>2</sub>)

**OR**

2. **Air** – in Type 2 respiratory failure (raised PaCO<sub>2</sub>)
Nebulised drugs for acute exacerbations should be switched back to inhalers as soon as possible. Patients should be stable on inhalers for at least 24 hours before discharge.

Long term nebuliser therapy is only required in a small minority of patients. Where it is being considered please refer to the Respiratory Specialist Nurse, Lung Function Department, UHL for full nebuliser assessment as an out-patient before decision made as to appropriateness.

Where long term treatment is necessary ensure appropriate equipment at home as an on-going loan/maintenance arrangement by the UHB equipment library. The patient must not be expected to purchase nebuliser equipment.

### 3.3 Acute asthma in adults

<table>
<thead>
<tr>
<th></th>
<th>Mild - Moderate</th>
<th>Acute severe</th>
<th>Life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEFR</td>
<td>&gt;50% of predicted</td>
<td>33-50% of predicted</td>
<td>&lt;33% of predicted</td>
</tr>
<tr>
<td>Speech</td>
<td>Normal</td>
<td>Unable to complete sentences</td>
<td>any of: silent chest, cyanosis, bradycardia, exhaustion or coma</td>
</tr>
<tr>
<td>Pulse</td>
<td>Normal ≤ 110 beats per minute</td>
<td>&gt;110 beats per minute</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>&lt;25 breaths/min</td>
<td>≥25 breaths/min</td>
<td></td>
</tr>
</tbody>
</table>

**Life-threatening asthma**

*British Guideline on the management of asthma, BTS/SIGN: May 2008 updated May 2011*

**Inform ITU.** Measure arterial blood gases. Start oxygen to maintain SpO₂ 94-98%. Salbutamol 5mg or terbutaline 10mg with ipratropium 500 micrograms (nebulised on 8L/min of oxygen). Oral prednisolone 40-50mg or IV hydrocortisone 100mg stat (or both if patient is very ill). Steroid tablets are as effective as the injection, provided that the tablets can be swallowed and retained. No sedatives of any kind.

**If there is no improvement after 15-30 minutes,** give nebulised beta₂-agonist more frequently e.g. salbutamol 5mg up to every 15-30 minutes or 10mg continuously hourly. **Notify Registrar to review urgently.** Continue nebulised ipratropium 500 micrograms 4-6 hourly.
If **improvement**, continue oxygen, give prednisolone 40-50mg po daily or IV hydrocortisone 100mg 6-hourly and continue nebulised beta\_2-agonist and ipratropium 4-6 hourly and step up usual inhaled steroid therapy.

If **patient still not improving**, discuss with senior clinician and ITU team.

**ONLY following consultation with senior medical staff:**

**IV magnesium sulphate**
Only in patients with acute severe asthma without a good initial response to inhaled bronchodilator therapy or those with life threatening or near fatal asthma.

- **Dose:** 1.2-2g
- **Administration:** Add to 100mL sodium chloride 0.9% and administer over 20 minutes
- **Consider use of IV aminophylline or IV beta\_2-agonist** (discuss with senior clinician).

**IV Aminophylline**
Avoid IV aminophylline in patients already taking oral aminophylline or theophylline unless plasma level is known to guide dosage.

- **Dose:** Loading dose of 5mg/kg administered slowly over 20 minutes (only if patient not had previous therapy)
  Maintenance dose of 500-700 micrograms/kg/hour as an infusion is usual. Levels should be taken if the patient remains on infusion for more than 24 hours.
- **Administration:** Add 500mg aminophylline to 500mL of glucose 5% or sodium chloride 0.9% to produce a 1mg/mL solution. Administer at 0.5-0.7mL/kg bodyweight/hour (refer to Appendix 1)

**IV Salbutamol**
- **Dose:** 4 micrograms/kg IV slowly over 5 minutes (with CVS monitoring). Can also be administered by infusion (see below) or 8 micrograms/kg SC or IM (repeated every four hours if necessary).
- **Administration:** Add salbutamol 5mg in 5mL to 500mL (to produce a 10 microgram/mL solution) of glucose 5% or sodium chloride 0.9%. Starting dose 5 micrograms/min (0.5mL/min) increasing cautiously to 15 micrograms/min (1.5mL/min) depending upon response.

**Acute severe asthma**
Start oxygen to maintain SpO\_2 94-98%: salbutamol 5mg or terbutaline 10mg nebulised on O\_2.
Oral prednisolone 40-50mg daily, for at least five days, or until recovery (or IV hydrocortisone 100mg 6-hourly).

**Monitor response at 15-30 minutes. If no improvement, treat as life-threatening.**
If improvement only slight, then repeat nebulised salbutamol / terbutaline with ipratropium bromide.
Respiratory System

If pulse and respiratory rate settling and PEFR >50% predicted continue 4-hourly nebulised salbutamol, daily oral prednisolone, and step up usual inhaled steroid therapy. If no improvement, treat as life-threatening.

**Uncontrolled asthma**

Salbutamol 5mg or terbutaline 10mg nebulised on O₂.
Monitor therapy after 15-30 minutes. If (a) PEFR 50-75% predicted, give oral prednisolone 40-50mg* and step up usual inhaled steroid therapy, or if (b) PEFR >75% predicted, step up usual inhaled steroid therapy. If for discharge, check inhaler technique (consider pharmacy involvement). Advise patient to visit their GP as soon as possible for review.

*Oral prednisolone should be continued for at least 5 days at 40-50mg (rarely 20mg in small, frail patients) until patient asymptomatic or back to his/her normal state. Patient should also show little or no nocturnal/early morning PEFR dip for at least 2 consecutive nights, and be established on high dose inhaled steroids.
3.4 Chronic asthma in adults

Stepwise approach (based on BTS/SIGN guidelines- revised January 2012)

In chronic asthma start at the step most appropriate to initial severity and aim to establish maintenance dose at the lowest level that controls symptoms. Control of symptoms is defined as: no daytime symptoms, no night time awakening due to asthma, no need for rescue medication, no exacerbations, no limitations on activity including exercise, normal lung function (in practical terms FEV₁ and/or PEFR > 80% predicted or best) with minimal side effects. Step up treatment as necessary and step down when control is good. Reductions in inhaled steroid dose should be considered every three months, decreasing the dose by approximately 25-50% each time. Before initiating a new drug therapy check compliance with existing therapies, inhaler technique and eliminate trigger factors. When deciding which drug to step down first and at what rate, the severity of asthma, the side effects of the treatment, time on current dose, the beneficial effect achieved, and the patient's preference should all be taken into account.

1. Occasional relief short-acting inhaled beta₂-agonist i.e. salbutamol 200 micrograms or terbutaline 500 micrograms 4 hourly prn. Check compliance and inhaler technique at each step. Consider whether poorly treated rhinitis is contributing to symptoms.

2. Add regular inhaled steroids at 200 to 800 micrograms per day if using relief beta₂-agonist three times a week or more; symptomatic three times a week or more; or waking one night a week. Consider inhaled steroids in patients who have had an exacerbation of asthma requiring oral corticosteroids in the last two years. Start at the dose of inhaled steroid appropriate to severity of disease.

In most adults a reasonable starting dose will usually be 400 micrograms/day Clenil or equivalent (e.g. Clenil 200 micrograms bd, Qvar 100 micrograms bd, budesonide 200 micrograms bd or fluticasone 100 micrograms bd).

3. Add inhaled long-acting beta₂-agonist (LABA e.g. salmeterol) if not controlled at step 2. Combination inhalers (e.g. Symbicort, Seretide or Fostair) are recommended to guarantee that the LABA is not taken without inhaled steroid and to improve inhaler adherence.

If benefit from LABA but control is still inadequate continue LABA but increase inhaled steroid dose to 800 micrograms/day (if not already on this dose). If no response to LABA-stop LABA and increase inhaled steroid dose to 800 micrograms/day.

If control still inadequate, then institute trial of other therapies e.g. leukotriene receptor antagonist or sustained release (SR) theophylline. The use of budesonide/formoterol in a single inhaler as rescue medication instead of a short-acting beta₂-agonist, in addition to its regular use as a controller treatment, is an effective treatment option. Before starting this careful patient education is required. Patients taking rescue budesonide/formoterol once a day or more should have their treatment reviewed.
Respiratory System

4. High dose inhaled steroid - up to 2000 micrograms/day (beclometasone dose or equivalent). Consider trials of addition of fourth drug e.g. leukotriene receptor antagonist, SR theophylline or oral beta<sub>2</sub>-agonist.

5. Add regular oral steroid (as a single daily dose - lowest dose that provides adequate control) if not controlled at step 4. Maintain high dose inhaled steroid at 2000 micrograms/day. Refer patient for specialist care.

Omalizumab may be considered for patients with severe allergic asthma meeting the necessary requirements. (NICE TA133) Consultant initiation only.

Full details on suggested inhaler choices can be found on the GP Referral & Pathway Guidance section of the intranet under the Asthma, COPD & Oxygen heading.

3.5 Chronic obstructive pulmonary disease (chronic bronchitis and emphysema)

*NICE Clinical Guideline 101, June 2010*

- Advise stop smoking (if patient agreeable refer to smoking cessation counsellor – see section 3.13), take exercise, reduce weight if overweight (as appropriate).
- Stepwise approach to COPD. Remember to assess the likely effects of any change and step down if appropriate.

1. Use short-acting bronchodilator as needed (beta<sub>2</sub>-agonist e.g. salbutamol/terbutaline or antimuscarinic e.g. ipratropium bromide).

2. In patients who remain breathless or have exacerbations, offer the following maintenance therapy:
   - FEV<sub>1</sub> ≥ 50% predicted: either long-acting beta<sub>2</sub>-agonist e.g. salmeterol/formoterol or long-acting antimuscarinic e.g. tiotropium (discontinue short-acting ipratropium & use salbutamol/terbutaline prn) If persistent exacerbations or breathlessness, consider switching salmeterol/formoterol to a corticosteroid-containing combination inhaler (e.g. Seretide or Symbicort)
   - FEV<sub>1</sub> < 50% predicted: either long-acting beta<sub>2</sub>-agonist with an inhaled corticosteroid in a combination inhaler (e.g. Seretide or Symbicort) or long-acting antimuscarinic e.g. tiotropium (discontinue short-acting ipratropium & use salbutamol/terbutaline prn).

3. If still symptomatic, consider using a long-acting antimuscarinic (e.g. tiotropium) alongside a combination inhaler (e.g. Seretide or Symbicort) irrespective of the FEV<sub>1</sub>

4. If an inhaled corticosteroid is declined or not tolerated, consider a long-acting antimuscarinic in addition to a long-acting beta<sub>2</sub>-agonist.

5. If still symptomatic, consider adding SR theophylline/ aminophylline (for therapeutic levels see Appendix 1).

Refer to chest physician at this stage for formal assessment and review of therapy.
Respiratory System

Patients should be offered pneumococcal vaccination and an annual influenza vaccination.

- For those patients whose chronic productive cough exacerbates symptoms consider trial of a mucolytic e.g. carbocisteine 750mg tds initially. Reduce to 750mg bd or 375mg qds after 2 weeks. Review treatment after 4 weeks and stop if no benefit.

- Maintenance use of oral corticosteroid in COPD is not normally recommended. Some patients with advanced COPD may require maintenance of oral corticosteroids when these cannot be withdrawn following an exacerbation. In these cases, the dose of oral corticosteroids should be kept as low as possible.

Full details on suggested inhaler choices can be found on the GP referral & pathway guidance section of the intranet under the Asthma, COPD & Oxygen heading.

3.6 Pulmonary Rehabilitation Therapy

- Once patient is on optimal therapy for their severity consider referral to UHL for Pulmonary Rehabilitation.

3.7 Tiotropium (Spiriva)

- Tiotropium is unsuitable for the acute treatment of bronchospasm – it takes 2 hours to reach peak effect from a single dose.

- If a patient is admitted with a COPD exacerbation, is already using tiotropium and requires nebulised treatment then
  i. In some patients e.g. those who do not have respiratory failure, salbutamol alone may be nebulised and tiotropium continued.
  ii. If the patient does not begin to improve in terms of breathlessness, chest tightness and/or blood gases with the above approach then nebulised ipratropium may be tried in addition to nebulised salbutamol and the tiotropium should be discontinued until the switch back to hand held inhalers is made.

- The full effect of tiotropium may take a number of days to develop so a transitional period with prn ipratropium (via nebuliser or inhaler) may be appropriate when reintroducing tiotropium.

In patients admitted to hospital who use regular nebulised ipratropium at home, consideration should be given to simplifying their medication once they are recovering from the acute exacerbation. At the point where hand-held inhalers would normally be reintroduced, once daily tiotropium 18 micrograms can be substituted for QDS nebulised ipratropium in those able to use the HandiHaler device. PRN ipratropium may be offered during the transition as above. If the switch is successful in terms of symptomatic control, it should be stressed to the patient and GP that this is to replace the nebulised ipratropium and is not in addition to it.
3.8 Acute exacerbations of COPD

Steroid therapy - prednisolone po 30mg daily for 7-14 days.

Bronchodilators
Salbutamol 2.5-5mg or terbutaline 5-10mg nebulised on air should be given on arrival and 4-6 hourly thereafter. Add ipratropium bromide 500 micrograms 6-hourly for severe exacerbations. In severe cases, nebulised bronchodilators may be given more frequently.

If no response, consider IV aminophylline (see section 3.3). Nebulised therapy should be continued for 24-48 hours and then consider switching to inhaled therapy. Nebulisers are rarely required long-term, unless for palliative reasons.

Antibiotics
- Consider antibiotics if
  1. Patient reports increase in purulence of sputum OR
  2. Pyrexia
  3. Consolidation on chest X-ray.
For antibiotic choices please refer to the MicroGuide

Consider diuretics and ventilatory support if appropriate. Discuss with senior colleagues.

3.9 Oxygen therapy

Acute setting
Oxygen therapy can be dangerous in certain patients, most notably those with chronic CO\textsubscript{2} retention. Follow guidelines for emergency oxygen prescribing in secondary care.

As with any drug it is a legal requirement that oxygen be prescribed for administration. However it can be given in acutely unwell patients without a prescription.
Oxygen should be prescribed on the pre-printed oxygen section of the drug chart (see next page) in order to keep saturations within a specified range. The majority of patients will require target saturations of 94-98%. Patients with Type 2 respiratory failure or those at risk of CO\textsubscript{2} retention should be prescribed a target saturation of 88-92%.
Decisions regarding long term oxygen therapy (LTOT): Patients should be referred to a respiratory clinic (THOR 50 is the code for this clinic) for review within 6 to 8 weeks unless the oxygen prescription is for palliative purposes (no referral required).

Oxygen therapy in acute exacerbations (see also section 3.11)
If patient >50 years of age or has a history of type 2 respiratory failure, select target saturations of 88-92% and do not give oxygen greater than 28% at 4L by Venturi mask (or 2L via nasal cannulae) until the arterial blood gases are known. Blood gases must be rechecked within 60 minutes of every change in inspired oxygen concentration and within 60 minutes of starting oxygen therapy.

If the PaO$_2$ is responding and PaCO$_2$ not risen by > 5mmHg above normal or initial raised value, the inspired oxygen concentration may be increased until the oxygen saturations are >90% (PaO$_2$ > 57mmHg or 7.6kPa).

If patients have an elevated PaCO$_2$ do not increase oxygen saturations above 92% because hypoxic drive will be lost and CO$_2$ retention will worsen. Consider non-invasive ventilation or referral to chest physician or intensivist.
3.10  Oxygen Devices - Guideline for emergency oxygen use in adult patients

Controlled oxygen therapy
Accurate concentration of oxygen can be given. For example: Venturi mask: A 28% (white) mask/tubing will always give 28% oxygen, as long as the minimum flow rate is 4L/min. Only applies to Venturi mask and Respiflow devices.

<table>
<thead>
<tr>
<th>DEVICE/FiO₂</th>
<th>INDICATIONS</th>
<th>ADVANTAGES</th>
<th>LIMITATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venturi mask</td>
<td>Safe for Type 2 respiratory failure</td>
<td>Accurate</td>
<td>Claustrophobic and expensive</td>
</tr>
<tr>
<td>FiO₂ 24-60% Fixed rate 24% 2L/min blue, 28% 4L/min white, 35% 8L/min yellow, 40% 12L/min red, 60% 15L/min green.</td>
<td>COPD patients 24-28%</td>
<td>Colour coded barrels.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Also good for those needing higher oxygen delivery.</td>
<td>Fixed FiO₂ not affected by respiratory rate or depth. No rebreathing.</td>
<td></td>
</tr>
<tr>
<td>Respiflow</td>
<td>As above</td>
<td>As above. Can be used in patients with tracheostomy Humidified</td>
<td>Noisy</td>
</tr>
<tr>
<td>FiO₂ 28-100% Fixed rate Flow rate stated on wall mounted venturi</td>
<td>High Flow Oxygen</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Non controlled oxygen therapy
With these devices you can only estimate what % oxygen a patient will receive. These may vary between devices. For example, a patient receiving 4L/min via nasal cannula will be receiving approximately 36% oxygen. However a patient receiving 4L/min via an MC mask will be receiving approximately 40% oxygen.

<table>
<thead>
<tr>
<th>DEVICE/FiO₂</th>
<th>INDICATIONS</th>
<th>ADVANTAGES</th>
<th>LIMITATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal cannulae</td>
<td>Patients with Type 1 and Type 2 respiratory failure (at max 2L/min for Type 2 patients). Good for Long Term Oxygen Therapy (LTOT). <strong>Do not use</strong> for patients who require high percentage oxygen e.g. MI, acute asthma.</td>
<td>No re-breathing. Low cost and easy for patient to eat and talk.</td>
<td>Not precise delivery, less delivery if mouth breathing. Dries the nose, can cause headaches. FiO₂ - 24-40% only. Depends on respiratory rate, depth of breathing and geometry of nose.</td>
</tr>
<tr>
<td>Low Flow, FiO₂ varies, 24-40% 1L/min approx. 24% 2L/min approx. 28% 4L/min approx. 36% Variable 2L/min 28% (up to 40%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium concentration mask</td>
<td>Patients with Type 1 Respiratory failure (never Type 2). Use for patients who need high oxygen concentrations: asthma, pneumonia, CCF, PE 40-60% <strong>Do not use with COPD patients</strong></td>
<td>Useful in mouth breathers, nasal irritation, epistaxis.</td>
<td>Patients can rebreathe their expired CO₂ with these masks (at low flow rates i.e. &lt;5L/min). FiO₂ depends on flow setting, mask fitting and patient's breathing</td>
</tr>
<tr>
<td>FiO₂ 40-60% Very variable rate 2L/min approx. 29% 4L/min approx. 40% 6L/min approx. 53% 8L/min approx. 60%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The table below shows APPROXIMATE conversion values.

<table>
<thead>
<tr>
<th>Device/FiO₂</th>
<th>Indications</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-re-breathing mask (High flow)</td>
<td>Mostly used in trauma, shock, severe asthma, large PE to give highest percentage oxygen. Do not use with COPD patients, unless for resuscitation</td>
<td>If this device is used in error at low flow rates it will cause re-breathing of CO₂ (&lt;6L/min). Only use in Critical Care.</td>
<td></td>
</tr>
<tr>
<td>FiO₂ 60-100% depending on flow rate (minimum 6L/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Guidance for titrating oxygen up and down as determined by saturations

### Titrating Oxygen up and down

This table below shows APPROXIMATE conversion values.

<table>
<thead>
<tr>
<th>Device Type</th>
<th>FiO₂ (%)</th>
<th>Flow Rate (L/min)</th>
<th>Recommended Oxygen Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venturi</td>
<td>24% (blue)</td>
<td>2-4</td>
<td>Nasal specs 1L</td>
</tr>
<tr>
<td>Venturi</td>
<td>28% (white)</td>
<td>4-6</td>
<td>Nasal specs 2L</td>
</tr>
<tr>
<td>Venturi</td>
<td>35% (yellow)</td>
<td>8-10</td>
<td>Nasal specs 4L</td>
</tr>
<tr>
<td>Venturi</td>
<td>40% (red)</td>
<td>10-12</td>
<td>Simple face mask 5-6L/min</td>
</tr>
<tr>
<td>Venturi</td>
<td>60% (green)</td>
<td>12-15</td>
<td>Simple face mask 7-10L/min</td>
</tr>
<tr>
<td>Reservoir mask at 15L oxygen flow</td>
<td>seek medical advice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reservoir mask required</td>
<td>seek senior medical input immediately</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Long Term Oxygen Therapy (LTOT)**

All patients to be prescribed home short burst or long term oxygen therapy (SBOT or LTOT) should be reviewed by a respiratory specialist (SpR, consultant or CRRU specialist). CRRU contact details Ext. 25092 or UHW pager 07623619731. Follow guidelines for stable oxygen prescribing in secondary care.

**Home Oxygen Guidance**

For patients newly initiated on home oxygen, a Home Oxygen Order Form (HOOF A) must be completed by the requesting clinician. Fax the completed form to the CRRU Home Oxygen Service at UHL (029 2071 6431). Once reviewed, CRRU will alert the prescriber to go ahead and fax the HOOF A to Baywater Healthcare (formerly called Air Products), GP and LHB. A Home Oxygen Consent Form (HOCFw) must also be completed. Most patients already on LTOT will have concentrators, so no need for further action at admission/discharge.

Please inform CRRU of any patients admitted with pre-existing oxygen (SBOT & LTOT) to ensure they are followed-up in oxygen clinic.

The removal of pre-existing oxygen for patients admitted to hospital should only be arranged if the patient is not expected to return home or if they are a long-term inpatient.

Full guidance on home oxygen and all forms (HOOF A /HOCFw) can be found on the Home Oxygen Service intranet page [Home Oxygen](#).
3.11 Emergency Oxygen Prescribing Guidelines in Secondary Care

**Patients at risk of hypercapnic (ventilatory) failure:**
- Moderate/severe COPD
- Chest wall deformity
- Neuromuscular disease
- Obesity (esp BMI>40)
- Bronchiectasis and CF

**Mandatory:**
Take a blood gas in all critically ill patients and those at risk of ventilatory failure.

**Mandatory:**
Record inspired oxygen (FiO\(_2\)) on blood gas request form and in notes.

**Mandatory:**
All patients with respiratory acidosis should be discussed with SpR/Consultant.

Oxygen is a treatment for hypoxaemia and not breathlessness in the absence of hypoxaemia.

Is the patient critically ill?
- Yes
  - Reservoir mask Oxygen 15L/min or bag-valve mask
- No
  - Patient at risk of hypercapnic respiratory failure?
    - Yes
      - Target sats 94-98%
    - No
      - Target sats 88-92%

24% or 28% FiO\(_2\) via venturi + ABG

- pH <7.35 and PCO\(_2\) >6KPa (45mmHg)
- pH >7.35 and PCO\(_2\) >6KPa (45mmHg)
- pH >7.35 and PCO\(_2\) <6KPa (45mmHg) and no previous hypercapnoea

Refer for NIV Keep sats 88-92%
Target sats 88-92%

Hyperoxia has been shown to result in worse outcomes in patients with mild-moderate stroke, post myocardial infarction and post neonatal resuscitation. Only in CO poisoning is hyperoxia required.

Oxygen should be prescribed on the drug chart according to target sats. Use oxygen stickers in the interim before drug chart is changed.

Adapted from British Thoracic Society guidelines Thorax 2008, 63; supplement 6
3.12 Stable Oxygen Prescribing Guidelines in Secondary Care

All patients to be prescribed home oxygen (SBOT or LTOT), should be reviewed by a respiratory Specialist (SpR, Consultant or CRRU specialist)

Home oxygen should be prescribed where possible in a stable setting as an outpatient.

LTOT (long term oxygen therapy) is oxygen >15 hours/day
SBOT (short burst oxygen therapy) is oxygen for short periods after exercise (<2 hours/day)

Any patients sent home on LTOT should have a blood gas on the oxygen flow rate that they are being discharged with. Ensure PCO₂ rise <1KPa

Respiratory follow up is necessary to ensure an accurate diagnosis and that oxygen is required

HOOF (home oxygen ordering form) can be found on the Home Oxygen Service intranet page. See details in section 3.10 for where to send completed forms.
3.13 Smoking cessation

Advice and help in giving up smoking can be obtained from the Smoking Cessation Counsellor in UHW Ext 43582 or UHL Ext 25420. The use of pharmacological aids in this area should be discussed with the counsellor.

As a result of the relevant NICE publications Cardiff and Vale UHB has developed the following procedure for the provision of Nicotine Replacement therapy (NRT), bupropion and varenicline.

All patients who smoke should be asked if they want to stop smoking and if the answer is yes support for smoking cessation should be offered to all patients (especially those with cardiovascular and/or respiratory conditions and for obstetric patients). It should be included in care pathways and pre-admission checklists for elective surgery or cardiology investigation and treatment.

- NRT, bupropion or varenicline should normally only be prescribed within the UHB’s smoking cessation support programme which includes advice and support (counselling). Medical, nursing or pharmacy staff can refer patients to the smoking cessation counsellor (see above).
- NRT will be issued to patients AFTER an assessment has been made on the appropriateness of such therapy and the patient has been referred for Smoking Cessation support. For in-patients the counsellor will “prescribe” the NRT on the in-patient medication chart, indicating NICE 39 in the “Pharmacy/Supply” box.
- A 24-hour NRT patch will be used first line (these may be removed after 16 hours if nicotine exposure must be limited e.g. pregnancy).
- NRT lozenges or gum are available for those patients with relevant skin conditions and for those who smoke >25/day.
- If the counsellor decides that varenicline (Champix) or bupropion (Zyban) is a suitable option then the medical team will be requested to prescribe this on the in-patient medication chart, indicating NICE 39 in the pharmacy/supply box.
- The counsellors will arrange regular follow-up and support of the patient. They will validate claims of quitting by measurement of expired air carbon monoxide at 4 weeks, 3 months, 6 months and one year.
- NRT or other smoking cessation therapies are NOT indicated for alleged nicotine dependence unless the patient is referred to the smoking cessation counsellor for support.
- Patients admitted on NRT (and requesting continuation while in hospital) will only be issued further supplies if they are referred to the smoking cessation counsellor for support.
- Only nicotine lozenges/patches/gum will routinely be issued. Other forms of NRT therapy (inhalator, Microtabs, mini lozenge, nasal spray or oral spray) are significantly more expensive and should only be used in exceptional circumstances. Patients admitted on these products and wishing to continue will be encouraged to obtain existing supplies from home in the first instance before hospital supply is considered. They may still be seen by the counsellor and entered in the follow up programme.
3.14 Emergency treatment of anaphylactic reactions in adults
Resuscitation Council UK, 2008

Anaphylactic reaction?

Airway, Breathing, Circulation, Disability, Exposure

Diagnosis – look for:
- Acute onset of illness
- Life-threatening Airway and/or Breathing and/or Circulation problems
- And usually skin changes

- Call for help
- Lie patient flat
- Raise patient’s legs

Adrenaline

When skills and equipment available:
- Establish airway
- High flow oxygen
- IV fluid challenge
- Chlorphenamine
- Hydrocortisone
- Monitor:
  - Pulse oximetry
  - ECG
  - Blood pressure

1 Life-threatening problems:
  Airway: swelling, hoarseness, stridor
  Breathing: rapid breathing, wheeze, fatigue, cyanosis, SpO₂ < 92%, confusion
  Circulation: pale, clammy, low blood pressure, faintness, drowsy/coma

2 Adrenaline (give IM unless experienced with IV adrenaline)
  IM doses of 1:1000 adrenaline (repeat after 5 min if no better)
  - Adult: 500 micrograms IM (0.5 mL)
  - Child more than 12 years: 500 micrograms IM (0.5 mL)
  - Child 6-12 years: 300 micrograms IM (0.3 mL)
  - Child less than 6 years: 150 micrograms IM (0.15 mL)
  Adrenaline IV to be given only by experienced specialists
  Titrate: Adults 50 micrograms; Children 1 microgram/kg

3 IV fluid challenge:
  Adult: 500–1000mL
  Child: crystalloid 20mL/kg
  Stop IV colloid if this might be the cause of anaphylaxis

4 Chlorphenamine (IM or slow IV)
- Adult or child more than 12 years: 10 mg
- Child 6-12 years: 5 mg
- Child 6 months to 6 years: 2.5 mg
- Child less than 6 months: 250 micrograms/kg

5 Hydrocortisone (IM or slow IV)
- Adult or child more than 12 years: 200 mg
- Child 6-12 years: 100 mg
- Child 6 months to 6 years: 50 mg
- Child less than 6 months: 25 mg
3.15 Chemical pleurodesis with talc slurry

This procedure should only be done in patients under the care of a respiratory or thoracic surgical consultant.

Indications

Recurrent symptomatic malignant pleural effusion.
Recurrent secondary pneumothorax (not fit for surgical intervention).

General preparation

Review chest x-ray to ensure that pleural effusion has been drained and that lung has adequately expanded.

Should be <150mL drainage in the past 24 hours.

Ensure that drain is patent.

Wherever possible, ensure that steroids and non-steroidal anti-inflammatory drugs (including aspirin) have been withheld for 48 hours pre- and post-procedure.

Patient preparation

Explain procedure to patient.
Obtain written consent.
Explain possibility of pain, pyrexia and (rarely) pneumonitis.

Premedication

Give 5-10mg oral morphine (Oramorph) 15 minutes prior to procedure (optional).

If patient very anxious consider giving 0.5-2mg midazolam IV 5 minutes prior to procedure (this is rarely needed). Monitor respiratory rate and oxygen saturation.

Procedure

Instil 20mL 1% lidocaine or 12mL 2% lidocaine through the chest drain.
Turn off the three-way tap while preparing the talc slurry.

Make up 4g sterile talc in 40mL sodium chloride 0.9% in a 50mL syringe.
Agitate to ensure thorough mixing.

Draw up a 20mL sodium chloride 0.9% flush into a separate syringe.

Agitate mixture prior to instilling talc slurry slowly and gently over a couple of minutes.

Flush drain with 20mL sodium chloride 0.9% and turn off tube.
Observe for pain/distress.

Clamp drain for 2 hours and then open.

Treat any mild pyrexia with paracetamol. Treat pain promptly, opiates may be required.

Remove drain when drainage <150-200mL in 24 hours.
CHAPTER 4 CENTRAL NERVOUS SYSTEM

4.1 Acute pain

- Strong/weak opioids, non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol act at different points in the pain pathway. Combining agents increases efficacy and minimises side effects; this is not the same as switching between agents, which is frequently ineffective. Regular analgesia is invariably more effective than PRN analgesia.

- Always use the oral route where possible.

- **Co-codamol** is available with paracetamol 500mg and either 8mg or 30mg codeine. Specify which is required: co-codamol 30/500 or co-codamol 8/500.

- **NSAIDs** are very effective and sometimes cheap pain killers. They are the analgeses of first choice in bone pain and following dental procedures. NSAIDs are best avoided in patients with a history of peptic ulceration and renal impairment. They should be used with caution in the elderly, in aspirin-sensitive asthmatics, in patients taking warfarin and the critically ill.

  - Ibuprofen 400mg tds is the first line NSAID, naproxen 250-500mg bd is second line.

  - Diclofenac suppositories may be used if the rectal route is more appropriate, NB Only use diclofenac after careful consideration in patients with cardiovascular risk factors such as high blood pressure, raised cholesterol, diabetes and smoking. Do not use in patients with ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or established heart failure (NYHA II-IV) *(MHRA Drug Safety Update June 2013)*

- Co-prescription of a proton pump inhibitor (PPI) (e.g. omeprazole 20mg daily) should be considered as gastric protection if:
  - Using the maximum recommended dose of a NSAID
  - Aged 65 years or older
  - History of gastroduodenal ulcer, GI bleeding or gastroduodenal perforation.
  - Concomitant use of medications that are known to increase the likelihood of upper GI adverse events (e.g. anticoagulants, aspirin [even low dose], corticosteroids, and antidepressants [e.g. selective serotonin reuptake inhibitors, venlafaxine])
  - Review need for PPI when stopping NSAID

- Most of these drugs are available as soluble tablets or liquids for those with swallowing difficulties only. Paracetamol and diclofenac are also available as suppositories.

- Never use pethidine, unless morphine is contraindicated – pethidine is shorter acting and there is a maximum 24 hour dose limit of 1g. More than this can lead to fitting due to norpethidine toxicity.

- Never prescribe the same dose of intramuscular (IM) morphine or IM pethidine intravenously (IV). These drugs are approximately 3-4 times more potent when
Central Nervous System

given by the IV route. Always state a dose interval and maximum daily dose.

- All patients prescribed intravenous opioids should have frequent observations (pulse, BP, respiratory rate, $O_2$ sats) along with assessments of pain, nausea and sedation, as per appropriate protocol.
- Always ensure naloxone and cyclizine are prescribed when strong opioids e.g. morphine, pethidine, are being used – therefore ensure patient has IV access.

**Always use a stepped approach to analgesia:**

**Pain on movement:**

<table>
<thead>
<tr>
<th>Mild</th>
<th>Treat with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paracetamol 1g (PR/PO) qds</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate</th>
<th>Codeine 30mg and Paracetamol 500mg (or co-codamol 30/500) 2 tabs qds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+/- Ibuprofen 400mg tds (if no contraindications)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe</th>
<th>Codeine 30mg and Paracetamol 500mg (or co-codamol 30/500) 2 tabs qds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+/- Ibuprofen 400mg tds (if no contraindications)</td>
</tr>
<tr>
<td></td>
<td>+/- e.g. Oral morphine 5-10mg pm 1 hourly</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>Oral paracetamol 1g qds (see section 4.1.1)</td>
</tr>
<tr>
<td></td>
<td>Oral morphine 5-10mg 4 hourly (regularly)</td>
</tr>
<tr>
<td></td>
<td>Oral morphine 5-10mg 1 hourly prn for breakthrough pain</td>
</tr>
<tr>
<td></td>
<td>+/- Naproxen 250mg - 500mg bd</td>
</tr>
<tr>
<td></td>
<td>+/- Morphine 7.5mg or 10mg IM as per hourly algorithm</td>
</tr>
<tr>
<td></td>
<td>(available on surgical wards)</td>
</tr>
</tbody>
</table>
4.1.1 Prescribing of paracetamol

- Weight must be documented on in-patient drug chart BEFORE paracetamol is given.

- For convenience of measurement the following doses are recommended:

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>Recommended paracetamol dose in 24 hours (adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-39kg</td>
<td>500mg qds</td>
</tr>
<tr>
<td>40-49 kg</td>
<td>750mg qds</td>
</tr>
<tr>
<td>50kg or above</td>
<td>1g qds</td>
</tr>
</tbody>
</table>

- A minimum dosage interval of 4 hours (6 hours in renal impairment) should be observed.

- This approximates to a total daily dose of 60mg/kg and is applicable to oral, IV and rectal routes.

- Remember co-codamol and co-dydramol preparations contain paracetamol. Consider prescribing components separately.

4.1.2 Oxycodone (OxyNorm, OxyContin)

Oxycodone is available as a 4-hourly immediate-release preparation (OxyNorm capsules/liquid) and as a 12-hourly sustained release preparation (OxyContin). All patients should be commenced on oral morphine as first line treatment. If however, the patient develops side-effects with morphine (e.g. hallucinations, itching or rash) then switching to oxycodone may be appropriate. Please refer to section 4.1.3 for prescribing opioids in severe renal impairment.

Please refer to table on opioid dose equivalencies, section 4.3.

4.1.3 Opioid prescribing for patients with severe renal impairment (eGFR < 30mL/min)

All opioids must be prescribed with caution in renal impairment; start with lower dose, escalate slowly and monitor patient closely to reduce risk of adverse events.

Morphine prescribing is complicated by the fact its main active metabolite has a significant degree of urinary excretion so patients with renal impairment are at high risk of opioid-related side effects due to drug accumulation. Such problems may not be immediately apparent and are a particular problem with chronic therapy, even at small doses.
Central Nervous System

**Patients with severe renal impairment**
*(eGFR 15-29mL/min, i.e. Chronic Kidney Disease stage 4)*

Morphine can be prescribed 1st line but:
- Initiate with 50% of normal starting dose.
- Initiate at reduced frequency (every 6 hours or every 8 hours).
- Escalate dose with great care (e.g. 25% dose increments every 48 hours).
- Monitor closely for signs of opioid toxicity.
- Review regimen if renal function deteriorates.
- Overall, have low threshold for switching to low dose oxycodone or reconsider a weaker opioid.

Oxycodone (with its alternative pharmacokinetic profile) is a potential alternative for patients with an eGFR <30mL/min if intolerant of morphine.

**Patients with established renal failure**
*(eGFR <15mL/min, i.e. Chronic Kidney Disease stage 5 including patients on dialysis)*

Oxycodone can be prescribed 1st line, acknowledging the fact that all strong opioids must be prescribed cautiously for patients with renal impairment.
4.2 Recommendations for the treatment of phantom limb pain

If phantom limb pain is diagnosed early postoperatively, **commence** intravenous infusion of calcitonin, 200 units/day for two days (unlicensed indication). **Use in combination with basic analgesia.**

Does phantom limb pain still exist?

- **YES**
  - No further intervention required

- **NO**
  - Anticonvulsants: If no contraindication commence gabapentin 300mg nocte. (Refer to BNF re contraindications/interactions) and increase as per protocol (see section 4.4) until optimal analgesia achieved, or intolerable side effects, maximum dose usually 1800mg/day.

  Is phantom limb pain acceptable?

  - **YES**
    - Continue with current regimen

  - **NO**
    - If patient has found some benefit from gabapentin continue, otherwise reduce gradually. Please seek weaning advice from the Acute Pain Service

Tricyclic antidepressants If no contraindication commence amitriptyline 10mg nocte. Increase as per protocol (see section 4.4) until intolerable side effects/effective pain management occurs, maximum dose usually 75mg od. (Refer to BNF re: contraindications/interactions)

Is phantom limb pain acceptable?

- **YES**
  - Continue with current regimen

- **NO**
  - Oral opioids Titrate opioid until optimal analgesia achieved, or intolerable side effects occur. Change to slow-release opioid if no contraindication.

  Is phantom limb pain acceptable?

  - **YES**
    - Continue with current regimen

  - **NO**
    - Refer to Acute Pain Service
4.3 Systematic approach to chronic non-malignant pain management

Analgesic Ladder

Regular oral Paracetamol

Regular weak opioid
e.g. Codeine,

Ineffective

Nil by mouth

Intolerant or ineffective because of swings in drug levels

Consider ONLY where oral route not appropriate – dementia, non-compliance, swallowing problems.

Slow Release prep.
Dihydromorphine SR, Tramadol SR

Intolerant or ineffective

Strong Opioid

Morphine (MST)
Start at 5mg bd. Can titrate up to 30mg bd

Ineffective

Butrans patch
5 micrograms/hour

Morphine (MST)
Start at 5mg bd. Can titrate up to 30mg bd

Intolerant

Oral oxycodone
MR (Oxycontin)
Up to 20mg bd

Intolerant or nil by mouth

Fentanyl patch
Up to 25 micrograms/hour

If ineffective, consider referral to pain specialist

Butrans patch
10 micrograms/hour

Ineffective

Review – is oral route now available / appropriate?

NO

Fentanyl patch
Up to 25 micrograms/hour

Intolerant or Ineffective

Butrans patch
5 micrograms/hour

Ineffective
Central Nervous System

- to be used in conjunction with accompanying Practice Tips

Post-herpetic neuralgia

Lidocaine 5% patch

If ineffective or intolerant STOP

Neuropathic component

Duloxetine

If ineffective or intolerant. For diabetic neuropathy only

Amitriptyline

Intolerant or ineffective

Partial effect

ADD

STOP

Gabapentin

Intolerant or ineffective and localised pain

Capsaicin cream 0.075%

Intolerant or ineffective

Pregabalin

Inflammatory component

Oral ibuprofen

Ineffective

Localised pain

Topical ibuprofen

Ineffective

Naproxen

Strong opioids should not be used as first line pain therapy if other evidence based interventions are available, and should only be used if appropriate for the patient.

1. Please also see section 4.4
Management of Chronic Non-Malignant Pain
Practice tips (to supplement section 4.3 Systematic approach to chronic non-malignant pain management)

General notes
1. The goal of therapy should be to reduce symptoms sufficiently to support improvement in physical, social and emotional functioning.
2. Ensure a pain assessment tool is used (e.g. Brief Pain Inventory). The same tool used at the patient’s initial assessment should be used throughout to ensure consistency.
3. Patients with chronic pain should be fully involved with their treatment. Patients should be provided with advice and information to promote self-management. Non pharmacological methods should always be considered alongside the algorithm.
4. Patients with chronic pain should be prescribed regular pain control. Strong opioids should only be used in slow release form. Immediate release opioids for breakthrough pain are only required, if at all, when moving from one step to another.
5. When moving from one step to the next, ensure an adequate trial of at least 5 days at an appropriate dose. This will allow transient side effects to diminish and the effectiveness of the step to be assessed.
6. Only one change at a time should be made to the drug regimen. This allows each change to be assessed appropriately.
7. Some patients find paracetamol ineffective for chronic pain and would rather not be taking up to 8 extra tablets each day. In such circumstances, it would be reasonable to stop and re-assess pain after at least 5 days.
8. For full prescribing information, refer to the individual summary of product characteristics (SPCs) for each drug. http://www.medicines.org.uk/emc/

Opioids
9. Opioids are useful in decreasing chronic pain to manageable levels. Complete pain relief is rarely achieved.
10. Strong opioids should not be used as first line pain therapy if other evidence based interventions are available, and should only be used if appropriate for the patient.
11. The following are common side effects of opioids:
   - Nausea: this is usually short term and a regular antiemetic, such as cyclizine, could be prescribed for the first few days
   - Constipation: consideration should be given to prescribing a laxative (a stimulant and softener) to be taken on a regular basis
   - Drowsiness: this is usually short term and the patient should be re-assured (and educated regarding driving)
   Continue opioids for adequate time to allow transient side effects to diminish.
12. Caution must be exercised when rotating from one strong opioid to another (see dose equivalence chart). As some patients may find one opioid more effective than another, it is usual to start below the equivalent dose and titrate slowly until effective or until maximum recommended dose is reached.
13. Opioid doses in chronic non-malignant pain should not be escalated beyond doses suggested within the dose equivalence table (see next page). These are much smaller doses than those associated with malignancy. If a patient does not achieve useful relief of pain at maximal doses of opioids within the pathway, they should be referred to a specialist pain service.

For further guidance see: “Opioids for Persistent Pain - Good Practice” British Pain Society

Neuropathic pain (see also section 4.4)
14. When prescribing amitriptyline, advise patient to take at 1900-2000hrs to avoid hangover effect.

15. In some patients side effects may be less profound with amitriptyline, gabapentin and pregabalin if dose titration is slower. This is more likely to improve patient compliance in persevering with the line of treatment to optimal effect. Printed schedules for slow titration are available from the Pain Team or Pharmacy.

16. Capsaicin may require up to 4–6 weeks regular application to achieve an effect. If allodynia is present, the patient will also require initial analgesic cover with a local anaesthetic cream such as EMLA or Ametop.

17. It has been agreed that no patients in Cardiff and Vale UHB should be initiated on lidocaine patches unless it is for the licensed indication of post-herpetic neuralgia. If there are exceptional circumstances for newly prescribing lidocaine patches then the appropriate Clinical Board Director will need to approve use and it is then the responsibility of the prescriber to communicate this to the patient’s GP for ongoing review and supply.

18. Patients already on lidocaine patches should be reviewed, using the chronic pain algorithm, and switched to appropriate alternatives where possible. Patient information leaflets on the use and review of lidocaine patches are available from ward pharmacists.

19. Lidocaine patches should be applied to unbroken skin for “12 hours on, 12 hours off” at the site of local pain. If more than one site is involved the patch can be cut. In rare circumstances more than one patch may be required.

NSAIDs
20. As many patients may be at risk of adverse events associated with NSAIDs, such as acute renal failure, gastro-intestinal toxicity, and an increased risk of cardiovascular events, the topical route could be considered ahead of the oral route for localised pain of an inflammatory nature.
Opioid prescribing – Chronic Non-Malignant Pain – Dose equivalence

<table>
<thead>
<tr>
<th>Dose level</th>
<th>Codeine Total daily dose</th>
<th>Dihydro-Codeine Total daily dose</th>
<th>Tramadol Total daily dose</th>
<th>MST (morphine sulphate) Total daily dose</th>
<th>Fentanyl patch Changed every 3 days</th>
<th>BuTrans patch buprenorphine Changed weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30-60mg</td>
<td>30-60mg</td>
<td>50-100mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60-120mg</td>
<td>60-120mg</td>
<td>100-200mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>120-180mg</td>
<td>120-180mg</td>
<td>200-300mg</td>
<td>10mg</td>
<td></td>
<td>5 micrograms/hr</td>
</tr>
<tr>
<td>4</td>
<td>240mg</td>
<td>240mg</td>
<td>300-400mg</td>
<td>20mg</td>
<td></td>
<td>10 micrograms/hr</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>30mg</td>
<td>12 micrograms/hr</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>60mg</td>
<td>25 micrograms/hr</td>
<td></td>
</tr>
</tbody>
</table>

All figures for oral preparations are for TOTAL DAILY DOSE. These are not exact equivalent doses, but give a guide for clinical practice.

NB 10mg oral morphine is equivalent to 5mg oral oxycodone.

Caution must be exercised when rotating from one strong opioid to another. As some patients may find one opioid more effective than another, it is usual to start below the equivalent dose and titrate slowly until effective or until maximum recommended dose is reached.
4.4 Neuropathic pain

Amitriptyline
Initial dose - 10mg nocte increased to 25mg nocte followed by 50mg nocte up to a maximum of 75mg nocte. The intervals in between dose titration will vary according to patient response and side effects.

OR
Gabapentin
Day 1 300mg nocte
Day 2 300mg bd
Day 3 300mg tds
Day 4 300mg am
300mg midday
600mg nocte
Day 5 600mg am
300mg midday
600mg nocte
Day 6 600mg tds

- If pain relief is significantly better at any stage during the course of treatment then maintain patient on the current dose.
- If pain continues carry on with regime.
- The rapid dose increase schedule above is suitable for inpatients where side effects (e.g. drowsiness) can be easily monitored. A slower titration schedule, more suitable for outpatients, is available from Pain Team or Pharmacy.
- If side effects occur reduce dose and contact the Acute Pain Team.
- Increase dose every 3 days in patients who are unwell, elderly or who have deranged creatinine and electrolytes.
- Consider using a smaller dose in patients who are frail and/or have chronic renal impairment.
- Management of neuropathic pain is reviewed in NICE CG173, November 2013.
- Local expert opinion consensus is that gabapentin should still be used before pregabalin.
- Local expert opinion is that amitriptyline should still be used first line in preference to duloxetine (60-120mg od) for diabetic neuropathy.

4.5 Night sedation

- In general, night sedation should be avoided since benzodiazepines may lead to physical and psychological dependence. They should be used to treat insomnia only if it is severe, disabling or subjecting the individual to distress, for a maximum of 2 to 4 weeks.
- Before prescribing a hypnotic, ensure that treatable causes of sleeplessness such as pain, depression, anxiety and confusion are appropriately managed.
Regulating sleep is an important part of management of affective disorders, in particular bipolar illness, and due attention should be given to treating insomnia in these patients.

Remember that the elderly normally sleep fewer hours than the young. Do not initiate regular hypnotics in the elderly.

If initiating a hypnotic, always prescribe PRN and review regularly especially at discharge. Never initiate regular night sedation in a patient of another team – write as a stat dose.

If a hypnotic is initiated in hospital then it is best practice not to include it in the patient’s discharge medication (although there may be some exceptional circumstances particularly with psychiatric patients).

The NICE Appraisal 77, April 2004 (zaleplon, zolpidem and zopiclone for the short-term management of insomnia) recommends that the drug with the lowest purchase cost should be prescribed because of a lack of compelling evidence to distinguish between them e.g. zopiclone or the shorter-acting benzodiazepine hypnotics.

Temazepam 10-20mg is appropriate for most patients (5mg may be appropriate in the elderly). Counsel them about the addictive properties first. Temazepam is a schedule 3 controlled drug.

Promethazine, a sedating antihistamine, can also be useful for the treatment of insomnia.

4.6 Acute confusion

Diagnosis of an acute confusional state (properly termed delirium) requires the identification of a disturbance of consciousness or attention, and a deficit in cognition (memory, orientation or language) that is different from the patient’s usual baseline mental state. It is particularly common in elderly patients. The most common cause of acute confusion in the elderly is infection. Drugs such as anticholinergics, antipsychotics, benzodiazepines, opioids and others can also precipitate delirium.

Treating symptoms without exclusion and treatment of the underlying cause is inappropriate, and usually unsuccessful.

Humane restraint may be necessary to protect the patient and medication may need to be a part of this. Pharmacological measures are not without risk, and should be used with caution.

All antipsychotics can cause cardiovascular depression and should be used with caution and only as a last resort, particularly in the elderly. It is probably better to be familiar with one or two drugs and use lower doses in the elderly.

Quetiapine 25mg nocte orally (unlicensed indication) can be used for persistent agitation and confusion in the elderly and especially for recurrent evening exacerbation gradually increasing, as required, in line with the following treatment algorithm:
Day 1 - quetiapine 25mg nocte
Day 2 - review and increase to 25mg bd if no improvement
Day 3 - review and increase to 25mg mane, 50mg nocte if no improvement
Day 4 - review and if no improvement increase to 50mg bd.

- Lorazepam 0.5-1mg bd-qds prn orally for agitation (in elderly - maximum 2mg in 24 hours) may be used as a second line option where necessary.

- In individuals where access is only available parenterally, lorazepam can be given either IM or IV 0.5-1mg bd-qds prn (in elderly - maximum 2mg in 24 hours)

- Haloperidol 2.5mg IM may be used. The effect of haloperidol will need to be reviewed after an hour to decide whether repeated dosage is necessary. Oral and IM procyclidine should be available in case of an acute dystonic reaction. (note the SPC for haloperidol now recommends that a baseline ECG should be done prior to treatment in all patients)

- All pharmacological measures need to be kept under constant review. Most patients will be able to stop treatment; continued medication will slow rehabilitation and increase risk of falls.

4.7 Alcohol withdrawal

- Patients should ideally be detoxified using diazepam ‘symptom triggered therapy’ (S-TT) based on the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). Using this protocol, patients often need less diazepam and also for a shorter time. Diazepam should be written on the prn side of the in-patient drug chart with a dose of 20mg and ‘as per CIWA’ in the frequency box with 200mg maximum 24-hour dose.

  NB CIWAs should only be used by nurses who are familiar with the procedure.

- Pabrinex *

  *In Whitchurch Hospital, Pabrinex IM is used – please refer to local guidance

- For prescribing of thiamine supplementation for the prophylaxis and treatment of Wernicke’s (WKS) refer to clinical guideline.

- The use of antipsychotic agents (e.g. haloperidol) is no longer recommended for alcohol withdrawal symptoms (haloperidol was previously recommended for the treatment of psychotic symptoms associated with delirium tremens).

- Neuroleptic agents have the potential to cause a variety of serious adverse effects (e.g. lowering of seizure threshold, acute dystonia, prolongation of QT-interval, hypotension and sudden death), especially when used in large doses which may be needed to control extreme agitation.

4.8 The management of status epilepticus in adults

- Treatment begins early in the development of status epilepticus. Treat seizures lasting more than 5 minutes; or more than one seizure without return of consciousness between seizures.
• Investigate aetiology when time permits but do not delay treatment to do this.
• Consider a non-epileptic cause for seizures.
• Organise blood testing for glucose, biochemistry, toxicology and drug levels.
• Please see algorithm for the management of status epilepticus.
Algorithm for the management of status epilepticus

* Note: The pathway allows for a maximum of 2 doses of benzodiazepine including doses given pre-hospital. Repeated doses of benzodiazepines are not indicated in the management of status epilepticus.

Secure airway
Assess cardiac and respiratory function
High flow oxygen
Check blood glucose level and correct if hypoglycaemic
Secure venous access in a large vein

Venous access
No venous access

Lorazepam *
4mg IV bolus (Note time)

If no response within 10 minutes

Lorazepam
4mg IV bolus (Note time)

Prepare phenytoin infusion
If no response within 10 minutes of lorazepam

Phenytoin intravenous infusion (see 4.8.1) and note time (BP & ECG monitoring, an inline filter and use of a large or central vein).
Alert anaesthetist

If convulsive seizures continuing 10 minutes after starting phenytoin

Contact anaesthetist

General anaesthesia as appropriate preferably with EEG monitoring

Midazolam oral liquid (unlicensed use) 10mg into buccal cavity (5mg in the elderly or body weight < 50kg) (Note time)

Establish venous access

If no venous access after 10 minutes

Establish venous access.

Repeat midazolam dose (Note time).

If venous access not possible
4.8.1 Phenytoin administration in management of status epilepticus

<table>
<thead>
<tr>
<th>Patient’s approximate weight in kg</th>
<th>Phenytoin dose in milligrams</th>
<th>Millilitres of sodium chloride 0.9% w/v required</th>
<th>Infusion time in minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-44</td>
<td>800</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>45-49</td>
<td>900</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>50-54</td>
<td>1000</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>55-59</td>
<td>1100</td>
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<td>25</td>
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<tr>
<td>60-64</td>
<td>1200</td>
<td>150</td>
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</tr>
<tr>
<td>65-69</td>
<td>1300</td>
<td>150</td>
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</tr>
<tr>
<td>70-74</td>
<td>1400</td>
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<td>30</td>
</tr>
<tr>
<td>75-79</td>
<td>1500</td>
<td>150</td>
<td>30</td>
</tr>
<tr>
<td>80-84</td>
<td>1600</td>
<td>200</td>
<td>35</td>
</tr>
<tr>
<td>85-89</td>
<td>1700</td>
<td>200</td>
<td>35</td>
</tr>
<tr>
<td>90-94</td>
<td>1800</td>
<td>200</td>
<td>40</td>
</tr>
<tr>
<td>95-99</td>
<td>1900</td>
<td>200</td>
<td>40</td>
</tr>
<tr>
<td>100 and over</td>
<td>2000</td>
<td>200</td>
<td>40</td>
</tr>
</tbody>
</table>

Phenytoin should not be commenced if seizures have stopped; but should be completed if seizures stop during the infusion.

**Practical guidance on administering phenytoin infusion** (refer also to the *Injectable Medicines Guide*)
- Use a large vein or central line
- Use a 0.22-0.5 micron inline filter
- Blood pressure and ECG monitoring
- Flush line with sodium chloride 0.9% w/v before and after administering phenytoin
- Cautions: hypotension, heart failure, respiratory depression
- Contraindications: sinus bradycardia or heart block, acute porphyria

Maintenance doses of phenytoin po 100mg tds (or IV if oral route not available) should be given following the loading dose.

Phenytoin plasma concentrations must be monitored (refer to appendix 1).

Phenytoin is not routinely recommended as a long term anti-epileptic drug. Seek senior advice regarding need for continued therapy and appropriate anti-epileptic drug choice.
4.9 **Drug-induced dystonic reactions**

Dystonic reactions can be caused by dopamine antagonists such as phenothiazines and antiemetics (e.g. metoclopramide). Treatment is with anticholinergic medication:

- *mild reaction* – procyclidine (oral) 5mg every 4 hours, maximum dose 30mg in 24 hours.
- *severe reaction* – procyclidine 5-10mg IM. Repeat if necessary after 30 minutes (elderly - preferably lower end of range)
4.10 **Guidelines for the sedation of violent patients**

(for treatment of acute agitation in patients in Whitchurch Hospital please refer to Rapid Tranquilisation Policy)

**Aims**
- To reduce distress for the patient.
- Reduce risk to others by maintaining a safe environment.

**Treatment Plan**
- Plans for the management of individual patients should normally be made in advance.
- A combination of:
  - Nursing levels / interventions
  - Placement
  - Pharmacological

**Emergency Situations**

<table>
<thead>
<tr>
<th>Action</th>
<th>If these means are unsuccessful</th>
<th>Offer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talking down</td>
<td></td>
<td>Oral LORAZEPAM 2-4mg</td>
</tr>
<tr>
<td>Time out</td>
<td></td>
<td>(sedation in 30-45 minutes, peaks in 1-3 hours, lasts 4-6 hours)</td>
</tr>
<tr>
<td>Extra nursing staff</td>
<td></td>
<td>Max. 4mg in 24 hours</td>
</tr>
<tr>
<td>Placement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Reminder**
- at this point consider
  - Consulting a senior colleague
  - Reviewing patient’s legal status

Monitor respiration rate, pulse, BP as often as possible
Wait a minimum of 45 minutes to assess response
Use benzodiazepines alone if any cardiac disease

If the patient refuses oral medication / consider other options

**Consider**

**IM Lorazepam 2-4mg**
(sedation in 30-45 mins. As above)
+ / -
**IM Haloperidol 2.5mg initially,**
rising to 5-10mg if necessary
(acts in 1-2 hours and lasts 18-24 hours)

**BNF recommended maximum dose = 18mg in 24 hours**

Aim to calm the patient, not sedate into unconsciousness

**Reminder**
- at this point consider
  - Consulting a senior colleague
  - Reviewing patient’s legal status

Take care injecting IM into a struggling patient

Monitor respiration rate, pulse, BP

**Nursing Observations**

After emergency sedation:
- Pulse
- Blood pressure
- Respiration
- Temperature

**Must be monitored**
Frequency to be decided by the prescribing doctor in consultation with nursing staff.
4.11 Prescribing to drug or substance misusers

The prescribing of any drug that has the potential for misuse to a patient known to misuse or is suspected of misusing drugs is potentially fraught with problems. This policy is designed to minimise the inappropriate prescription of drugs to this group of patients. This policy should not be used to discriminate against patients who may have a dependence problem.

- **Emergency Unit prescribing**
  The EU must not be seen to be an alternative source of drugs for the short term ‘treatment’ of substance dependence. Therefore if a patient, presenting to EU is known to misuse or is suspected of misusing drugs, be extremely cautious before prescribing or administering any drug that has the potential for misuse. Obviously these patients should be prescribed the analgesia appropriate to their clinical needs and may receive simple analgesia such as NSAIDs or paracetamol plus antibiotics etc as appropriate.

  If medical staff are concerned regarding pain assessment of an individual, advice from a senior colleague should be sought because of the potential of drug misuse/abuse.

  Unless there is a compelling clinical reason, avoid prescribing or issuing a prescription for:

  - **Any opioid** (includes codeine, dihydrocodeine, tramadol, methadone, co-codamol, co-dyramol, etc)
  - **Any benzodiazepine** (includes temazepam, diazepam, etc)

  EU does not have a role in detoxification programmes or withdrawal treatment. Patients should only be prescribed short term supplies of drugs to help with withdrawal symptoms or to replace lost medication. In these cases a senior doctor should assess the patient and the patient’s GP should be contacted.

- **Inpatient prescribing**
  If a patient, known to misuse or suspected of misusing drugs, is admitted to a ward, exercise caution before prescribing or administering any drug that has the potential for misuse.

  If the patient requires pain relief, non-opioids +/- NSAIDs should be considered as ‘first line’. Use of opioids for pain relief requires careful consideration and should only be used in appropriate clinical situations.

  **Be cautious before prescribing any substance liable to misuse to a patient who claims to receive it on prescription** (e.g. methadone or diazepam from the Community Addiction Unit or their own GP). It is strongly recommended that the doctor obtains verification of the drug/dose before the drug is prescribed.

  The Community Addictions Unit Clinic Co-ordinator can be contacted for patient details: Cardiff 2046 1742 (Monday–Thursday 9am–5pm, Friday 9am-4.30pm).

  Advise clinic of amounts prescribed as in-patient and on discharge so community supplies can be adjusted appropriately.
Outside of these hours, do NOT administer or prescribe any drug liable to misuse (particularly methadone) at the patient’s request, even if it means the patient suffers a withdrawal reaction. It is safer to manage withdrawal reactions than give the incorrect drug/dose of a potent opiate until full details of the patient’s drug therapy have been confirmed with the prescribing consultant who is organising the patient’s rehabilitation programme.

Do not prescribe regular doses of methadone or buprenorphine if the last dose was taken more than 3 days prior to admission. Tolerance will be reduced during this time, therefore refer to specialists for advice on restarting.

Methadone has a narrow therapeutic window (potential for respiratory depression and death) and the prescribing of methadone should only be by medical staff with appropriate training and knowledge of the drug. Both diazepam and methadone have long half lives, and as a result their pharmacological activity will persist for a long time.

- **Symptomatic treatment of opioid withdrawal**

Any patient withdrawing from opioids may obtain symptomatic relief with appropriate non-opioid drugs:

- Abdominal cramps: hyoscine butylbromide 20mg qds.
- Diarrhoea: loperamide 4mg stat then 2mg as needed following loose stool bowel movement up to a maximum of 16mg/24 hours.
- Muscle and joint pain: ibuprofen 400-600mg up to qds or naproxen 250-500mg bd.
- Anxiety and agitation: diazepam 10mg tds prn for a maximum of three days. This should be offered in addition to any regular dose that the patient is prescribed in the community.
- Nausea and vomiting: metoclopramide 10mg tds.

These should be prescribed in the “as required” section. Medication used to manage opioid withdrawal should be offered for approximately three to five days and should not be continued on discharge.

**4.12 Amitriptyline**

- Amitriptyline is prescribed frequently in ITU predominantly for its sedative properties.

- It is usually appropriate to stop amitriptyline when the patient is transferred to a general surgical/medical ward. First check that the patient was not taking amitriptyline prior to admission and taper the dose gradually.
4.13 Treatment of depression
NICE Clinical Guideline 90, October 2009

- First line use is a generic selective serotonin re-uptake inhibitor (SSRI), e.g. sertraline.

- SSRIs are as effective as tricyclic antidepressants (TCAs) and less likely to be discontinued because of side effects. However, if a patient has not responded following an adequate treatment trial, it is important to rule out non-compliance due to adverse effects (e.g. sexual dysfunction). Also consider:
  - the increased risk of bleeding with SSRIs; prescribe a gastroprotective drug for older people taking a non-steroidal anti-inflammatory drug or aspirin. Extra caution is advised for patients co-prescribed warfarin.
  - the risk of interactions with fluoxetine, fluvoxamine and paroxetine.
  - the higher incidence of discontinuation symptoms with paroxetine.
  - the use of citalopram or sertraline in patients with a chronic physical health problem, as these are associated with fewer drug interactions. Note however the potential for QT-interval prolongation with citalopram and its contraindication with other drugs with the potential to prolong the QT-interval.

- Other antidepressants e.g. TCAs, monoamine oxidase inhibitors (MAOIs), venlafaxine - consider:
  - toxicity in overdose in patients at risk of suicide. The greatest risk in overdose is with TCAs, except for lofepramine.
  - venlafaxine is associated with a greater risk of death from overdose compared to other antidepressants used in primary care.
  - the increased likelihood of discontinuation due to adverse effects; increase doses gradually with TCAs, venlafaxine and duloxetine.
  - the specific cautions, contraindications and monitoring requirements for individual drugs.
  - non-reversible MAOIs, antidepressant combination therapy and lithium augmentation should only be prescribed by specialist mental health professionals.

  Do not prescribe dosulepin.

- Cautions and counselling - when initiating treatment inform patients:
  - of the gradual development of full antidepressant effect over 4-6 weeks
  - of potential adverse effects and drug interactions some of which (e.g. nausea with SSRIs) will resolve with ongoing treatment
  - about the risk of discontinuation symptoms on stopping abruptly
  - to take medication regularly and continue beyond remission to reduce the risk of relapse
  - that antidepressants are not associated with addiction
Central Nervous System

- **Response to treatment**
  - If there has been minimal or no response after 3 to 4 weeks of treatment (6 to 8 weeks in the elderly) at a therapeutic dose, check compliance and consider increasing the dose or switching to another antidepressant.
  - If there is some improvement by 4 weeks, continue for another 2 to 4 weeks.

- **Consider switching antidepressants if:**
  - response is still not adequate or
  - there are adverse effects or
  - the person requests a change of drug

### 4.14 Treatment of Anxiety

*NICE Clinical Guideline 113, January 2011*

**Panic disorder**

- Do not prescribe benzodiazepines for the treatment of individuals with panic disorder.

- If drug treatment is necessary use an SSRI licensed for panic disorder e.g. citalopram, or if an SSRI is unsuitable or there is no improvement, imipramine or clomipramine may be considered.

**Generalised anxiety disorder**

- Benzodiazepines should not usually be used beyond 2 to 4 weeks.

- If drug treatment is necessary or preferred consider an SSRI. Paroxetine, venlafaxine and duloxetine are licensed for the treatment of generalised anxiety disorder (venlafaxine is more dangerous in overdose).

- Advise patients that symptoms of anxiety may worsen on initiation of an SSRI, but that they should continue treatment to ensure a therapeutic effect.

- Venlafaxine should not be prescribed for patients with uncontrolled hypertension.

- Blood pressure should be checked on venlafaxine initiation and regularly during treatment, particularly during dosage titration. Discontinue venlafaxine or reduce the dose for patients who experience a sustained increase in blood pressure.

- Monitor patients prescribed venlafaxine for signs and symptoms of cardiac dysfunction. Do not prescribe for patients with a high risk of serious cardiac arrhythmias or who have had a recent myocardial infarction.
CHAPTER 5 INFECTIONS

ATTENTION!

THIS SECTION IS OBSOLETE –

PLEASE REFER TO THE MICROGUIDE
6.1 Sliding scale insulin

This is a suggested scale which may need review and alteration to accommodate varying patient insulin requirements.

50 units Actrapid insulin in 50mL sodium chloride 0.9% - given IV via a syringe driver

<table>
<thead>
<tr>
<th>Blood glucose (hourly)</th>
<th>Infusion rate (units per hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4mmol/L</td>
<td>0</td>
</tr>
<tr>
<td>4.1-7.9mmol/L</td>
<td>1 unit/hour</td>
</tr>
<tr>
<td>8.0-11.9mmol/L</td>
<td>2 unit/hour</td>
</tr>
<tr>
<td>12.0-17.9mmol/L</td>
<td>3 unit/hour</td>
</tr>
<tr>
<td>18.0-27.9mmol/L</td>
<td>4 unit/hour</td>
</tr>
<tr>
<td>≥28.0mmol/L</td>
<td>Need medical review</td>
</tr>
</tbody>
</table>

*Note: administer with continuous glucose 5% with 0.3% potassium chloride 1L every 8 hours (for potassium administration in diabetic ketoacidosis see section 6.5.)*

- subcutaneous insulin is usually restarted when the patient is able to eat and should be given about one to two hours before the pump is discontinued.

6.2 Surgery in an individual with diabetes

Additional care is required to optimise glycaemic control, prevent hypo- and hyperglycaemia, and favour good wound healing and recovery. Aim for blood glucose of 5-13mmol/L in patients undergoing surgery, i.e. fasting blood glucose ≤8mmol/L or random blood glucose ≤15mmol/L. Local advice or guidance may be available, otherwise the following principles should be considered:

- All patients should continue their usual diabetes treatment on the day before surgery
- Type 2 (diet controlled) - treat as non-diabetic but monitor blood glucose.
- Type 2 (tablet) - if minor surgery: omit morning oral hypoglycaemic and monitor blood sugar.
- Type 2 (tablet) - if major surgery or poorly controlled: treat with insulin IV sliding scale on the day of surgery. Recomence oral hypoglycaemic agent when eating/drinking normally.
- Type 1 or Type 2 requiring long acting basal insulin - continue their normal dose.
- Type 1 or Type 2 requiring insulin - insulin IV sliding scale on the day of surgery. Recomence usual subcutaneous dose when eating/drinking normally.
Assessment for day surgery generally takes place at the initial outpatient consultation. Individuals with diabetes having surgery under local anaesthetic may attend the Day Surgery Units at UHW or UHL. Patients with diabetes are often not suitable for Day Surgery under general anaesthetic. Minor surgery may be considered if the patient has well controlled Type 2 diabetes. More detailed advice may be available locally.

Please also refer to Joint British Diabetes Societies (JBDS), April 2011 guideline (Management of adults with diabetes undergoing surgery and elective procedures: improving standards)
http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Surgery_Adults_Full.pdf
6.3 Treatment and management of hypoglycaemia in adults with diabetes mellitus in hospital

Hypoglycaemia is defined as blood glucose of less than 4mmol/L (if not less than 4mmol/L but symptomatic give a small carbohydrate snack for symptom relief)

**MILD**
- Patient conscious, orientated and able to swallow
- Give 3-5 tablets of GlucoTabs or 59ml GlucoJuice Liquid Blast
- Test blood glucose level after 15 minutes
- If still less than 4mmol/L, repeat above up to 3 times
- If this has been repeated 3 times, consider 10% glucose IV at 100mL/hr
  - Continue to test blood glucose every 15 minutes until >4mmol/L

**MODERATE**
- Patient conscious and able to swallow but confused, disorientated or aggressive
- If cooperative:
  - Ensure gag reflex is present
  - Give 1-2 tubes of GlucoGel/DextroGel
- If uncooperative:
  - Give 1mg Glucagon IM if suitable
  - Avoid in repeated hypos, NBM or severe hepatic disease
- Test blood glucose after 15 minutes, if still less than 4mmol/L, repeat up to 3 times.
- If this has been repeated 3 times, consider 10% glucose IV at 100mL/hr
  - Continue to test blood glucose every 15 minutes until >4mmol/L

**SEVERE**
- Patient unconscious/fitting or very aggressive or nil by mouth (NBM)
- Check ABC, stop any IV insulin and fast bleep a doctor
- If suitable give 1mg Glucagon IM (avoid in repeated hypos, NBM or severe hepatic disease) or give 10% glucose IV 150mL over 15 minutes.
- Test blood glucose after 15 minutes, if still less than 4mmol/L, repeat up to 3 times.
- If this has been repeated 3 times, consider 10% glucose IV at 100mL/hr
  - Continue to test blood glucose every 15 minutes until >4mmol/L

Blood glucose level should now be above 4mmol/L
- Give 20g of long acting carbohydrate eg. 2 biscuits or a slice of bread or next meal if due.
- If IM Glucagon has been used give 40g of long acting carbohydrate in order to replenish glycogen stores.

For enteral feeding patients ONLY: give 200mL milk (not soya) or restart feed or give 10% glucose IV at 100mL/hr

Blood glucose should now be above 4mmol/L. Follow up treatment as described on the left.
- If NBM start 10% glucose IV at 100mL/hr until no longer NBM or reviewed by doctor

Do not omit subsequent doses of insulin.
- Continue regular blood glucose monitoring four times a day for 48 hours or until stable.
- Give hypoglycaemia education or refer to diabetes specialist nurse for advice.
- Consider possible cause for hypoglycaemia and seek to prevent further episodes from occurring.
6.4 Treatment of hyperglycaemia

- Do not prescribe “PRN” doses of subcutaneous soluble insulin (e.g. Actrapid 6 units PRN if BM > 30). The risk of hypoglycaemia secondary to cumulative repeat doses outweighs the risk presented by isolated elevated blood sugars.

- Do not prescribe “stat” doses of insulin for Type 1 disease. Prescribe small increases in the dose of regular insulin or follow an approved IV insulin sliding scale regimen with documented arrangements for review.

- Seek expert advice if patient is acutely unwell. For urgent advice, out-of-hours, contact the on-call medical SpR.

- Refer patients with poor glycaemic control who are not acutely unwell to a diabetes specialist nurse.

- For all cases of hyperglycaemia consider contributing factors e.g. infection, poor compliance, poor drug delivery, drug interactions.

- See section 6.5 for the treatment of diabetic ketoacidosis and refer to section 6.6 for the treatment of hyperosmolar hyperglycaemic state (HHS)

6.5 Diabetic ketoacidosis (DKA)
(Joint British Diabetes Societies (JBDS) Inpatient Care Group March 2010)

Diabetic ketoacidosis is a severe metabolic disturbance which should be managed as a medical emergency.

Refer to link below for Cardiff and Vale UHB guidelines (based on those of JBDS) on clinical management


Immediate management: time 0 to 60 minutes

- Restoration of circulating volume is priority - commence sodium chloride 0.9% w/v
  - Systolic BP (SBP) below 90mmHg: Likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc. Give 500mL of sodium chloride 0.9% w/v over 10-15 minutes. If SBP remains below 90mmHg repeat whilst requesting senior input. Most patients require between 500 to 1000mL given rapidly. Consider involving the ITU/critical care team. Once SBP above 90mmHg give 1000mL sodium chloride 0.9% w/v over next 60 minutes. Addition of potassium likely to be required in this second litre of fluid.
  - Systolic BP on admission 90mmHg and over: Give 1000mL sodium chloride 0.9% w/v over first 60 minutes.
Potassium replacement:

<table>
<thead>
<tr>
<th>Potassium level (mmol/L)</th>
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<td>40mmol/L</td>
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<td>&lt; 3.5</td>
<td>senior review - additional potassium required</td>
</tr>
</tbody>
</table>

Commence a fixed rate intravenous insulin infusion (IVII)
- If weight not available from patient, estimate patient weight (in kg).
- Commence a fixed rate IVII via an infusion pump (50 units Actrapid made up to 50mL with sodium chloride 0.9%), but only after fluid therapy has commenced.
- Insulin weight-based fixed rate intravenous insulin infusion of 0.1 unit/kg/hour (i.e. 7mL/hr if weight is 70kg). Adjust in insulin resistant states if ketone concentration is not falling fast enough and/or the bicarbonate level is not rising fast enough.
- If the patient normally has subcutaneous long-acting insulin analogues e.g. Insulatard, insulin glargine, insulin detemir, then continue this at the usual dose and usual time (to avoid rebound hyperglycaemia when IV insulin is stopped).
- Insulin may be infused in the same line as the intravenous replacement fluid provided that a Y connector with a one way, anti-syphon valve is used and a large-bore cannula has been placed.

Assess patient: respiratory rate; temperature; blood pressure; pulse; oxygen saturation, Glasgow coma scale, full clinical examination.

Further investigations: capillary and laboratory glucose, venous blood glucose, creatinine and electrolytes, FBC, blood cultures, ECG, CXR, MSU.

Establish monitoring regimen:
- Hourly capillary blood glucose.
- Hourly capillary ketone measurement.
- Venous bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter.
- 4-hourly plasma electrolytes.
- Continuous cardiac monitoring if required, continuous pulse oximetry if required.

Consider any precipitating causes and treat appropriately.

60 minutes to 6 hours

Aims of treatment:
- Rate of fall of ketones of at least 0.5mmol/L/hr OR bicarbonate rise 3mmol/L/hr and blood glucose fall 3mmol/L/hr.
- Maintain serum potassium in normal range.
- Avoid hypoglycaemia.

Re-assess patient, monitor vital signs
- Hourly blood glucose (lab blood glucose if meter reading ‘HI’).
- Hourly blood ketones.
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter.
- If potassium is outside normal range, re-assess potassium replacement and check hourly. If abnormal after further hour seek immediate senior medical advice.

- Refer to previous potassium replacement table and if potassium greater than 3.5 and less than 5.5mmol/L continue fluid replacement via infusion pump as follows:
  - 1L sodium chloride 0.9% w/v with potassium chloride 40mmol/L (use ready mixed bags) over next 2 hours
  - 1L sodium chloride 0.9% w/v with potassium chloride 40mmol/L over next 2 hours
  - 1L sodium chloride 0.9% w/v with potassium chloride 40mmol/L over next 4 hours
  - Add glucose 10% 125mL/hr if blood glucose falls below 14mmol/L.
  - More cautious fluid replacement in young people aged 18-25 years, elderly, pregnant, heart or renal failure.

- Insulin infusion rate may need review if:
  - Capillary ketones not falling by at least 0.5mmol/L/hr
  - Venous bicarbonate not rising by at least 3mmol/L/hr
  - Plasma glucose not falling by at least 3mmol/L/hr
  - Continue fixed rate IVI until ketones less than 0.3mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18mmol/L.

- If ketones and glucose are not falling as expected always check the insulin infusion pump is working and connected and that the correct insulin residual volume is present (to check for pump malfunction). If equipment working but response to treatment is inadequate, increase insulin infusion rate by 1 unit/hr increments hourly until targets achieved.

- Additional measures
  - Regular observations and Early Warning Score (EWS).
  - Accurate fluid balance chart, minimum urine output 0.5mL/kg/hr.
  - Consider urinary catheterisation if incontinent or anuric (not passed urine by 60 minutes).
  - Nasogastric tube with airway protection if patient has impaired consciousness or persistently vomiting.
  - Measure arterial blood gases and repeat chest radiograph if oxygen saturation less than 92%.
  - Thromboprophylaxis with low molecular weight heparin (see chapter 2 section 2.34).
  - Consider ECG monitoring if potassium abnormal or concerns about cardiac status.

6 to 12 hours

- Ensure clinical and biochemical parameters improving.
- Continue IV fluid replacement.
  - Avoid hypoglycaemia.
  - Assess for complications of treatment e.g. fluid overload, cerebral oedema.
  - Treat precipitating factors as necessary.
Endocrine System

- Re-assess patient, monitor vital signs
  - If patient not improving seek senior advice.
  - Continue IV fluid via infusion pump at reduced rate
    - 1L sodium chloride 0.9% w/v with potassium chloride 40mmol/L over 4 hours
    - 1L sodium chloride 0.9% w/v with potassium chloride 40mmol/L over 6 hours
    - Add glucose 10% 125mL/hr if blood glucose falls below 14mmol/L
- Reassess cardiovascular status at 12 hours; further fluid may be required.
- Check for fluid overload.
- Review biochemical and metabolic parameters
  - At 6 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose.
  - Resolution is defined as ketones less than 0.3mmol/L, venous pH over 7.3 (do not use bicarbonate as a surrogate at this stage).
- Ensure referral has been made to Diabetes Inpatient Team.

12 to 24 hours
- Expectation: by 24 hours the ketonaemia and acidosis should have resolved. Request senior review if not improving.
- Aim:
  - Ensure that clinical and biochemical parameters are continuing to improve or are normal.
  - Continue IV fluid replacement if not eating and drinking.
  - If ketonaemia cleared and patient is not eating and drinking move to a variable rate IV as per local guidelines. Re-assess for complications of treatment e.g. fluid overload, cerebral oedema.
  - Continue to treat precipitating factors.
  - Transfer to subcutaneous insulin if patient is eating and drinking normally.
- Re-assess patient, monitor vital signs.
- Review biochemical and metabolic parameters.
- At 12 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose.
  - Resolution is defined as ketones <0.3mmol/L, venous pH>7.3.
  - If not resolved review fluid and insulin infusion.

Resolution of DKA
- Expectation: Patient should be eating and drinking and back on normal insulin.
- If DKA not resolved identify and treat the reasons for failure to respond. This situation is unusual and requires senior and specialist input.
- Transfer to subcutaneous insulin:
  - Convert to subcutaneous regime when biochemically stable (capillary ketones less than 0.3mmol/L, pH over 7.3) and the patient is ready and able to eat.
  - Do not discontinue intravenous insulin infusion until 30 minutes after subcutaneous short acting insulin has been given.
  - If the patient is newly diagnosed it is essential they are seen by a member of the Diabetes Inpatient Team, bleep 6502 (at UHW) prior to discharge.
6.6 Hyperosmolar hyperglycaemic state (HHS)

http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_HHS_Adults.pdf

- Seek senior advice to confirm treatment plan and review progress. Please also refer to full guideline.

- Usually presents with a longer history (e.g. a week), marked dehydration and marked hyperglycaemia (30mmol/L or more) without significant hyperketonaemia (<3mmol/L) or acidosis (pH >7.3, bicarbonate >15mmol/L). Osmolality usually 320 mosmol/kg or more.

- Use sodium chloride 0.9% w/v to restore circulating volume and reverse dehydration, initially using hourly osmolality measurements to guide adjustment of fluid replacement rate.

- Aim to replace approximately 50% of estimated fluid loss within the first 12 hours and the remainder in the following 12 hours. Rate of rehydration will be determined by assessing the combination of initial severity, degree of renal impairment and any pre-existing co-morbidities such as heart failure which may limit the speed of correction.

- If the osmolality is no longer declining despite adequate fluid replacement with sodium chloride 0.9% w/v AND an adequate rate of fall of plasma glucose is not being achieved (a fall in plasma glucose of between 4 and 6 mmol/hour is recommended) then sodium chloride 0.45% w/v should be substituted. It should be noted that an initial rise in sodium is expected and is not in itself an indication for hypotonic fluids. Thereafter, the rate of fall of plasma sodium should not exceed 10mmol/L in 24 hours.

- Commence an insulin infusion immediately ONLY if significant ketonaemia is present (3ß-hydroxy butyrate is more than 1mmol/L). Remember that patients may be more sensitive to insulin than in diabetic ketoacidosis (DKA). Start insulin at time zero and use a fixed rate intravenous insulin infusion given at 0.05 units per kg per hour (e.g. 4 units/hr in an 80kg man).

- A fall of glucose at a rate of up to 5mmol/L per hour is ideal. Once the blood glucose has ceased to fall following initial fluid resuscitation, reassess fluid intake and evaluate renal function. Insulin may be started at this point, or if already in place, increase the infusion rate by 1 unit/hr.

- A target blood glucose of between 10 and 15mmol/L is a reasonable goal in the first 24 hours. Complete normalisation of electrolytes and osmolality may take up to 72 hours.

- Patients with HHS are potassium deplete but less acidotic than those with DKA so potassium shifts are less pronounced. Potassium should be replaced or omitted as required (see table on next page).
Endocrine System

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- Patients with HHS are at high risk of venous thrombosis therefore prophylactic enoxaparin is advised. (See chapter 2 section 2.34)

6.7 Blood glucose testing –Type 2 diabetes mellitus – advice post discharge

- For patients with Type 2 disease who do not require insulin a fasting blood test in the morning before breakfast ONCE a week should be sufficient.
- Patients should be advised that, if unwell, they should test blood glucose up to four times a day before meals and at bedtime and seek medical advice if symptoms persist for longer than three days or if their blood sugar is more than twice its usual reading.

6.8 Investigations in an individual with diabetes (when fasting required)

e.g. IVP, barium meal, ultrasound of abdomen, CT head and neck.

Type 2 (diet controlled) - treat as non-diabetics.

On the day before the investigation:
  Type 2 (tablet controlled) - continue usual dose
  Type 1 or Type 2 requiring insulin - may require a reduced evening dose of intermediate/long acting insulin to prevent nocturnal or early morning hypoglycaemia.

On the day of the investigation:
  Type 2 (tablet) and fasted Type 1 or Type 2 requiring insulin – take/administer medication and food once investigation complete.

6.9 Investigations in an individual with diabetes (when bowel preparation is required)

e.g. barium enema

In addition to guidelines for fasting, the following steps are needed to avoid hypoglycaemia.

If possible, patients should monitor blood glucose FOUR times a day during the preparation period and on the day of the procedure.

Remind patient of signs of hypoglycaemia and what to do if this occurs.
• Type 2 (tablet controlled) - continue usual dose, supplement diet with clear, sugary fluids if required.
• Type 1 and Type 2 requiring insulin - maintain usual carbohydrate intake with clear, sugary fluids if required. Bowel preparation may take several days and this may require a corresponding reduction in insulin. On the day before the procedure a 30% reduction in the evening insulin dose may be required.

6.10 The management of Type 2 diabetes
NICE Clinical Guideline 87, March 2010, refer to www.nice.org.uk for further details.

Oral glucose control therapies
• Target HbA1c is 48mmol/mol (6.5%) but discussions with patients may mean that their individual HbA1c target is above this target.
• Measure HbA1c at 2-6 monthly intervals until the blood glucose is stable on unchanging therapy then measure at 6-monthly intervals (in Cardiff and Vale UHB HbA1c is measured every 3 months).

Metformin
• Metformin should be initiated in overweight or obese patients whose blood glucose is inadequately controlled by lifestyle interventions (nutrition and exercise) alone.
• Consider metformin as an option for first-line glucose-lowering therapy for patients who are not overweight.
• Titrate metformin dose up over a few weeks to minimise risk of gastrointestinal (GI) side effects. Consider a trial of extended-absorption metformin tablets where GI tolerability prevents continuation of metformin therapy.
• Review the dose of metformin if the serum creatinine exceeds 130 micromol/L or the estimated glomerular filtration rate (eGFR) is below 45mL/minute/1.73m^2.
• Stop the metformin if the serum creatinine exceeds 150 micromol/L or the eGFR is below 30mL/minute/1.73m^2.
• Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45mL/minute/1.73m^2.
• Patients should not receive metformin for 48 hours before and after contrast media.

Insulin secretagogues
• Consider a sulfonylurea (low cost but not glibenclamide) as an option for first-line glucose-lowering therapy if:
  the person is not overweight
  the person does not tolerate metformin (or it is contraindicated)
  or
  a rapid response to therapy is required because of hyperglycaemic symptoms.
• Add a sulfonylurea as second-line therapy when blood glucose control remains or becomes inadequate with metformin.
• Continue with a sulfonylurea if blood glucose control remains or becomes inadequate and another oral glucose-lowering medication is added.
• When drug concordance is a problem, offer a once-daily, long-acting sulfonylurea.
Dipeptidylpeptidase-4 (DPP-4) inhibitors (sitagliptin, saxagliptin)

- Consider adding a DPP-4 inhibitor instead of a sulfonylurea as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate (HbA1C greater than or equal to 48mmol/mol (6.5%) or other higher level agreed with the individual) if:
  - the person is at a significant risk of hypoglycaemia or its consequences (for example, older people and people in certain jobs (e.g. those working at heights or with heavy machinery) or people in certain social circumstances (e.g. those living alone)
  or
  - the person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated.

- Consider adding a DPP-4 inhibitor as second-line therapy to first-line sulfonylurea monotherapy when control of blood glucose remains or becomes inadequate (HbA1C greater than or equal to 48mmol/mol (6.5%), or other higher level agreed with the individual) if:
  - the person does not tolerate metformin, or metformin is contraindicated.

- Consider adding a DPP-4 as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate (HbA1C greater than or equal to 58mmol/mol (7.5%), or other higher level agreed with the individual) and insulin is unacceptable or inappropriate.

- Only continue the DPP-4 inhibitor therapy if the person has had a beneficial metabolic response (a reduction of at least 0.5 percentage points in HbA1C in six months).

Thiazolidinediones (glitazones)

- Consider adding pioglitazone instead of a sulfonylurea as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate (HbA1C greater than or equal to 48mmol/mol (6.5%), or other higher level agreed with the individual) if:
  - the person is at significant risk of hypoglycaemia or its consequences,
  or
  - a person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated.

- Consider adding pioglitazone as second-line therapy to first-line sulfonylurea monotherapy when control of blood glucose remains or becomes inadequate (HbA1C greater than or equal to 48mmol/mol (6.5%), or other higher level agreed with the individual) if the person does not tolerate metformin or metformin is contraindicated.

- Consider adding pioglitazone as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes
inadequate (HbA$_{1C}$ greater than or equal to 58mmol/mol (7.5%), or other higher level agreed with the individual) and insulin is unacceptable or inappropriate.

- Do not commence or continue pioglitazone in people who have heart failure or a history of heart failure or who are at higher risk of fracture. It should also not be used in patients with active bladder cancer or a past history of bladder cancer or in those who have uninvestigated macroscopic haematuria.

- Only continue thiazolidinedione therapy if the person has had a beneficial metabolic response (a reduction of at least 0.5 percentage points in HbA$_{1C}$ in six months).

**GLP-1 mimetic**


- Consider a GLP-1 mimetic in triple therapy regimens (in combination with metformin and a sulfonylurea, or metformin and a thiazolidinedione) when control of blood glucose remains or becomes unacceptable (HbA$_{1C}$ greater than or equal to 58mmol/mol (7.5%), or other higher level agreed with the individual), and the person has:
  
  a body mass index (BMI) greater than or equal to 35.0kg/m$^2$ in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight
  
or
  
a BMI less than 35.0kg/m$^2$ and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

- Only continue the GLP-1 mimetic if the person has had a beneficial metabolic response (a reduction of at least 1.0 percentage point in HbA$_{1C}$ and a weight loss of at least 3% of initial body weight at 6 months).

- Consider a GLP-1 mimetic in dual therapy regimens (in combination with metformin or a sulfonylurea) only if:

  the person is intolerant of either metformin or a sulfonylurea, or treatment with metformin or a sulfonylurea is contraindicated,

  and

  the person is intolerant of thiazolidinediones and DPP-4 inhibitors

  or

  a treatment with thiazolidinediones and DPP-4 inhibitors is contraindicated.

- Only continue the GLP-1 mimetic if the person has had a beneficial metabolic response (a reduction of at least 1.0 percentage point in HbA$_{1C}$ and a weight loss of at least 3% of initial body weight at 6 months).

**Oral agent combination with insulin**

- When starting basal insulin therapy:
Endocrine System

continue with metformin and the sulfonylurea
review the use of the sulfonylurea if hypoglycaemia occurs.

- When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):
  continue with metformin
  continue the sulfonylurea initially, but review and discontinue if hypoglycaemia occurs.

- Consider combining pioglitazone with insulin therapy for a person:
  - who has previously had a marked glucose-lowering response to thiazolidinedione therapy
  - on high-dose insulin therapy and whose blood glucose is inadequately controlled.
  Discontinue pioglitazone if clinically significant fluid retention develops.

Insulin therapy
- Start insulin therapy, with patient’s agreement, if individual target HbA1C not met
- Begin with human intermediate acting insulin, injected at bed-time or twice daily according to need.
- Consider, as an alternative, using a long-acting insulin analogue (insulin glargine, insulin detemir) if:
  - the person needs assistance from a carer or healthcare professional to inject insulin, and use of a long-acting analogue would reduce the frequency of injections from twice to once daily, or
  - the person’s lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes, or
  - the person would otherwise need twice-daily intermediate acting insulin injections in combination with oral glucose-lowering drugs, or
  - the person cannot use the device to inject the intermediate acting insulin.

- Consider twice-daily pre-mixed (biphasic) human insulin regimens particularly where HbA1C is greater than or equal to 75mmol/mol (9.0%). A once-daily regimen may be an option.

- Consider pre-mixed preparations that include short-acting insulin analogues rather than pre-mixed preparations that include short-acting human insulin preparations, if:
  - immediate injection before a meal is preferred, or
  - hypoglycaemia is a problem, or
  - blood glucose levels rise markedly after meals.

- Consider switching to a long-acting insulin analogue from intermediate acting insulin in people:
  - who do not reach their target HbA1C because of significant hypoglycaemia, or
  - who experience significant hypoglycaemia on intermediate-acting insulin irrespective of the level of HbA1C reached, or
- who cannot use the device needed to inject intermediate-acting insulin but who could administer their own insulin safely and accurately if a switch to a long-acting insulin analogue were made, or
- who need help from a carer or a healthcare professional to administer insulin injections and for whom switching to a long-acting insulin analogue would reduce the number of daily injections.

- Monitor a person using a basal insulin regimen (intermediate-acting or long-acting insulin analogue (insulin glargine, insulin detemir) for the need for short-acting insulin before meals (or a pre-mixed insulin preparation)

- Monitor a person who is using pre-mixed insulin once or twice daily for the need for a further injection of short-acting insulin before meals or for a change to a regimen of mealtime plus basal insulin, based on intermediate-acting insulin or long-acting insulin analogues, if blood glucose control remains inadequate.
### 6.11 Glycaemic control in Type 2 diabetes – prescribing pathway

**Step 1**

Lifestyle advice: Diet and Exercise
- refer to Dietetics for group education (XPRT) and also give the new “Advice for people newly diagnosed with Type 2 diabetes” booklet. Refer to DRSSW for retinal screening

<table>
<thead>
<tr>
<th>If HbA1c &gt; 48 mmol/mol (6.5%)</th>
<th>1st line treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 2</strong> Start Metformin</td>
<td></td>
</tr>
<tr>
<td>• 500mg od with food for 1 week, then 500mg bd for 1 week, increasing up to 500mg 2 bd if possible (£5.28 for 1000mg bd)</td>
<td></td>
</tr>
<tr>
<td>• If intolerant reduce dose and increase more slowly, encouraging to take at meal times</td>
<td></td>
</tr>
<tr>
<td>• If still intolerant try Metformin MR (£10.64 for 1000mg bd)</td>
<td></td>
</tr>
<tr>
<td>Reduce dose if eGFR 30-50mL/min; STOP if &lt; 30mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**Step 3** Add Sulfonylurea to Metformin (or vice versa)
- Gliclazide 40-80mg bd initially titrated to max 160mg bd (£5.24 for 160mg bd)
- Do not use Gliclazide MR unless compliance problem (£9.54 for max dose 120mg od)

**Step 4** Add basal insulin
- Human insulin 6-10 units am or pm and titrate according to fasting blood glucose
- Humulin I Kwikpen (£1.44 / 100units), Insulatard 3mL cartridge + Novopen (£1.53 / 100units), Insuman basal (£1.32 / 100 units)

Consider Lantus (£2.77 / 100 units) or Levemir (£2.80 / 100units) only if significant hypoglycaemia develops

**Alternative (2nd line) treatment options**

- • Consider sulfonylurea first line if BMI <28 or metformin contraindicated
- • Gliclazide 40mg bd titrated to 160mg bd (£5.24 for 160mg bd)

- • Change from sulfonylurea if hypoglycaemia or significant hypoglycaemia risk (see ‘other recommendations’) and consider:
  - Pioglitazone (£1.86 for 45mg od) or DPP4: Saxagliptin (£31.60)
  - Linagliptin (£33.26)
  - SGLT2: Dapagliflozin (£36.59) Canagliflozin (£100mg £36.58)
  - NB. Canagliflozin 300mg should not be used without specialist advice £46.66)
  - GLP-1 Exenatide: Byetta (£68.24) Bydureon (£73.36)
  - Liraglutide (1.2mg £78.48)

**Step 4**

- Alternatives to insulin if risk of hypoglycaemia or unable to inject safely
  - Pioglitazone, saxagliptin, linagliptin, dapagliflozin, canagliflozin, Byetta, Bydureon, Liraglutide
  - NB. Liraglutide 1.8mg dose should not be used as not NICE approved (£117.72)

If HbA1c > 59mmol/mol (7.5%) after 3-6 months trial of triple therapy
Step 5

**Add Prandial Insulin**

- If not already on insulin – start basal human insulin as above first or discuss with community consultant / diabetes nurse then:
- Add prandial insulin or switch to pre-mixed insulin
- **Stop sulfonylurea and pioglitazone**, if other oral treatments have been effective (see below) your community diabetologist may advise continuation although some drugs are unlicensed for this use (see individual SPC)
- Adding prandial human insulin **Humulin S 3mL cartridge** (£1.27 / 100 units) [Actrapid 3ml cartridge no longer available]
- Change to pre-mixed insulin **Humulin M3 Kwikpen** (£1.45 / 100 units), or **Insuman Comb 25 Solostar** (£1.32 / 100 units), or discuss with community consultant / diabetes nurse [Mixtard-30 3mL cartridge no longer available]

Review response to GLP-1, DPP-4 and SGLT-2 at 6 months, and:

Stop GLP-1 if less than 10mmol/mol (1.0%) drop in HbA₁c AND 3% drop in weight
Stop DPP-4 and SGLT-2 if less than 5mmol/mol (0.5%) drop in HbA₁c

**Other Recommendations**

- The flow chart represents standard practice and should be suitable for the majority of type 2 patients. It has been approved by the Diabetologists, Pharmacists and Primary Care representatives of C+V UHB.
- All newly diagnosed patients with diabetes should be referred for structured education and to the diabetic retinopathy screening service.
- HbA₁c targets should be individualised. Groups at risk of hypoglycaemia include those with erratic dietary patterns and those with tight glucose control.
- For the elderly/people with cognitive impairment refer to HbA₁c targets in the link below http://www.americangeriatrics.org/files/documents/ADA_Consensus_Report.pdf
- Hypoglycaemia avoidance paramount if occupation poses significant risk e.g. driving.
- Type 2 patients taking insulin are required to monitor their blood sugars before driving and should be prescribed test strips accordingly. Some will need to monitor frequently to avoid hypos.
- Type 2 patients not taking insulin will not usually need to monitor their blood glucose levels on a regular basis but may be encouraged to do so during ill health or if taking a sulfonylurea.
- In case of difficulty you are strongly advised to make contact with your community diabetologist or diabetes nurse in the first instance by email or telephone.
- NICE clinical guidelines provide more information and are available here: http://www.nice.org.uk/guidance/index.jsp?action=byTopic&o=7239
- Please note change to brand of needles on formulary. Mylife Pefine Classic and GlucoRx Finepoint replace previous formulary needles.

Costs for tablets and GLP-1s are for 28 days treatment. Costs for insulin are per 100 units. Costs from Oct 2014 Drug Tariff
6.12 Treatment notes – patients with Type 2 diabetes

*NICE Clinical Guideline 87, March 2010*

**Blood pressure management**
- BP target of <140/80mmHg (<130/80mmHg if there is kidney, eye or cerebrovascular damage).
- After lifestyle measures control BP with a generic angiotensin-converting enzyme (ACE) inhibitor first line (for people who are of African-Caribbean descent first-line treatment should be an ACE inhibitor plus either a diuretic or a generic calcium-channel blocker [CCB]).
- Substitute an angiotensin II-receptor antagonist if ACE inhibitor not tolerated (renal deterioration or hyperkalaemia are NOT valid reasons for switching).
- CCBs should be used first-line for a woman, if after an informed discussion, it is agreed there is the possibility of her becoming pregnant.
- Second line CCB or diuretic (usually bendroflumethiazide 2.5mg daily): third line add the other drug (i.e. the CCB or diuretic).
- Fourth line drugs are beta-blockers, alpha-blockers and potassium-sparing diuretics.

**Lipid management**

*NICE Clinical Guideline 87, March 2010 (please also refer to section 2.20-2.21)*

Consider a person to be at high premature cardiovascular (CV) risk for his or her age unless he or she: is not overweight, has a BP <140/80mmHg (in the absence of antihypertensive therapy), does not have microalbuminuria, does not smoke, does not have a high-risk lipid profile, has no history of CV disease (CVD) and has no family history of CVD.

- If CV risk >20% over 10 years in patients ≥40 years offer generic simvastatin (to 40mg*) or a statin of similar efficacy and cost.
- For patients <40 years old consider initiating generic simvastatin (to 40mg*) where the CV 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 CVD).
- Treat to target, total cholesterol <4.0mmol/L, or LDL-cholesterol, <2.0mmol/L.
- If target is not reached current practice is to switch to a more potent statin, rather than increasing to simvastatin 80mg daily.
- Consider intensifying cholesterol-lowering therapy (with a more effective statin or ezetimibe in line with NICE guidance) if there is existing or newly diagnosed CVD, or if there is an increased albumin excretion rate, to achieve a total cholesterol level below 4.0mmol/L (and HDL-cholesterol not exceeding 1.4mmol/L) or an LDL-cholesterol level below 2.0mmol/L. Treatment intensification with a more potent statin would be the preferred Cardiff and Vale UHB strategy for patients not at LDL targets.
- If high CV risk and triglyceride levels remain in the range 2.3-4.5mmol/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.

*note maximum dose of simvastatin is 20mg daily with concomitant amiodarone, verapamil, diltiazem or amlodipine and 10mg daily with concomitant fibrates (except fenofibrate)*

**Kidney damage**
- Start ACE inhibitor and titrate to full dose (if tolerated) in all individuals with confirmed raised albumin excretion rate (>2.5mg/mmol for men, >3.5mg/mmol for women). Maintain BP <130/80mmHg if abnormal albumin:creatinine ratio.

### 6.13 Withdrawal of corticosteroids

- The rate of withdrawal depends on duration of treatment, dose and whether the disease is likely to relapse as the dose of systemic corticosteroid is reduced.

- Withdrawal should not be abrupt in patients who have received systemic corticosteroids for greater than 3 weeks. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids, the dose may be reduced rapidly to physiological doses. Once a daily dose equivalent to 7.5mg of prednisolone is reached, dose reduction should be slower to allow the hypothalamo-pituitary-adrenal (HPA) axis to recover. If the disease is likely to relapse on corticosteroid withdrawal then clinical assessment of disease activity may be required during withdrawal.

- Abrupt withdrawal of doses of up to 40mg daily, or equivalent, for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression in the majority of cases (only appropriate if disease is unlikely to relapse).

In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:
- patients who have had repeated courses of systemic corticosteroids, particularly if taken for more than 3 weeks.
- when a short course has been prescribed within one year of cessation of long-term therapy (months or years).
- patients who may have other possible causes of adrenal suppression.
- patients receiving doses of systemic corticosteroid greater than 40mg daily of prednisolone (or equivalent).
- patients repeatedly taking doses in the evening.

### 6.14 Corticosteroid-induced osteoporosis

- For patients ≥65 years who have taken or are likely to take prednisolone for at least three months prescribe oral bisphosphonate (e.g. alendronic acid, risedronate).

Also refer for bone densitometry – to be requested via Medical Physics.
• For patients <65 years and taking prednisolone for at least three months, refer for bone densitometry (to be requested via Medical Physics). However if patient has already had a fragility fracture (e.g. vertebral crush) then prescribe oral bisphosphonate immediately.

Refer pre-menopausal women with glucocorticosteroid-induced osteoporosis, or at high risk of bone loss as a result of glucocorticosteroids, to the Bone Clinic.

• Calcium and vitamin D supplementation
Prescribe Calcichew D3 Forte one tablet once daily for all patients taking long term oral glucocorticosteroids (even if they are on oral bisphosphonate). Prescribe Calcichew D3 Forte one tablet twice daily if patient is not taking an oral bisphosphonate.

6.15 Primary prevention of osteoporotic fragility fractures

• Please refer to NICE TA160 (Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in post-menopausal women) and the National Osteoporosis Guideline Group (NOGG) Guidelines for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK.

6.16 Secondary prevention of osteoporotic fragility fractures

• In addition to the algorithm please also refer to NICE TA161 (Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women) and the National Osteoporosis Guideline Group (NOGG) Guidelines for the diagnosis and management of osteoporosis.

6.17 Strontium

• The use of strontium has been severely restricted following patient safety concerns highlighted by the MHRA and EMA. Use is precluded along with several co-morbidities often seen in postmenopausal women. The opportunity to critically review patients admitted on strontium should be undertaken. Advice on whether to stop treatment, alternatives if switching and circumstances when it is appropriate to commence strontium should be obtained from local specialists in osteoporosis care.
6.18 Secondary prevention of osteoporotic fragility fractures
Based on NICE TA 87, January 2005 – please refer also to NICE TA161

Postmenopausal women ≥ 1 clinically apparent fracture

- Age ≥ 75
  - Without the need for prior DEXA scanning
- Age 65-74
  - T-score -2.5 SD or below and where the presence of osteoporosis is confirmed by DEXA scanning
- Age < 65
  - T-score -3 SD or below OR
    - T-score -2.5 SD or below PLUS
    - ≥ 1 age independent risk factors

Oral Bisphosphonates (alendronic acid*, risedronate)

Unsatisfactory response or intolerant

- Age ≥ 65
  - T-score -4 SD or below OR
    - T-score -3 SD or below PLUS
      - Multiple fractures (>2) AND
      - ≥ 1 age-independent risk factors
  - Parathyroid hormone (teriparatide**)
- Selective oestrogen receptor modulators (SERMS) (raloxifene)
  - Contra-indicated or Physically unable to comply

* First line treatment option in most cases (available generically)
**NICE TA161 recommends teriparatide in women aged 55-64 years with a T-score of -4SD or below plus more than two fractures.
CHAPTER 7 OBSTETRICS, GYNAECOLOGY AND URINARY TRACT DISORDERS

7.1 Systematic approach to Overactive Bladder (OAB) management in adults

Please refer to the drug treatment algorithm for the management of overactive bladder in adults.
CHAPTER 9 NUTRITION AND BLOOD

9.1 Subcutaneous rehydration

- Subcutaneous rehydration is of particular use in frail patients who are unable to take adequate oral fluids, and in whom intravenous access may not be possible.
- Do not use to correct severe electrolyte disturbances.
- Patients with coagulation disorders may not be appropriate for this form of therapy.
- Patients with oedema and malnutrition will frequently be unable to absorb fluids administered subcutaneously.

Administration
- Insert butterfly subcutaneously into convenient part of the upper chest, behind the shoulders, or the anterior abdominal wall.
- This should be covered with a transparent dressing and inspected at least twice a day for signs of local infection.
- Change site if it becomes inflamed.

Suitable fluid
- The usual regimen is sodium chloride 0.9%, 1L over 12-24 hours.
- Patients in whom sodium chloride administration is inappropriate would probably warrant more careful monitoring of intravenous fluids and may, therefore, be inappropriate for subcutaneous hydration.
- Glucose 5%, glucose 4% and sodium chloride 0.18%, glucose 2.5% and sodium chloride 0.45% can be safely administered via this route.

Additives
- Potassium chloride 2g (27mmol) can be given in 1L of subcutaneous fluid. This is rarely needed. Use a ready mixed bag e.g. 0.2% strength potassium chloride infusion bag in sodium chloride 0.9% which contains 2g (27mmol) of potassium per litre. Patients with problems in potassium balance are inappropriate for subcutaneous fluids.
- Hyaluronidase (Hyalase) has been used to improve subcutaneous fluid absorption from the administration site, but this is rarely necessary. (If necessary 1,500 units may be dissolved in 1mL water for injection and added to 1L).

For all electrolyte abnormalities the cause should be elicited. For advice on investigating the cause contact the duty biochemist, UHW, Extension 48334, bleep 5452. Information on biochemistry assays can be obtained from the electronic “Laboratory Medicine Test Knowledge Base” available on the Clinical Portal.
9.2 Hypercalcaemia

- Rehydrate with 4 to 5L (consider 3-4L in the elderly, CRF and CCF) over 24 hours (IV +/- PO)

- Consider giving IV furosemide (and potassium if necessary). Discontinue, whenever possible, medicines known to cause or worsen hypercalcaemia e.g. thiazide diuretics.

- After rehydration and patient has passed urine give IV bisphosphonate (disodium pamidronate)

Table 1. Disodium pamidronate dose according to corrected serum calcium

<table>
<thead>
<tr>
<th>Corrected serum [Ca] (mmol/L)</th>
<th>Disodium pamidronate (max rate of administration 60mg per hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 3.0</td>
<td>15-30mg* in 100-250mL sodium chloride 0.9%</td>
</tr>
<tr>
<td>3.0 to 3.5</td>
<td>30-60mg* in 250-500mL sodium chloride 0.9%</td>
</tr>
<tr>
<td>3.5 to 4.0</td>
<td>60-90mg in 500mL sodium chloride 0.9%</td>
</tr>
<tr>
<td>&gt; 4.0</td>
<td>90mg in 500mL sodium chloride 0.9%</td>
</tr>
</tbody>
</table>

*higher dose to be added to largest fluid volume

Notes
- The infusion rate should never exceed 60mg/hour (1mg/min), and the concentration of disodium pamidronate concentrate in the infusion solution should not exceed 60mg/250mL. Disodium pamidronate maximum rate of administration is 20mg per hour in mild to moderate renal impairment.
- If corrected serum calcium is > 4.0, consider using salcetonin (calcitonin-salmon) 100-200iu tds (subcutaneous or intramuscular injection) for 2 days (higher doses may be necessary) as well as bisphosphonate.
- The total dose of pamidronate may be administered in a single infusion or in multiple infusions over 2-4 consecutive days. The maximum dose per treatment course is 90mg for both initial and repeated courses.
- Maintain hydration. A significant decrease in serum calcium is generally observed 24-48 hours after administration of pamidronate and maximal effect is usually seen after five days. If normocalcaemia is not achieved within this time, a further dose may be given.
- Consider measuring PTH if cause of the hypercalcaemia is unknown.

For further advice in the care of patients with hypercalcaemia of malignancy, contact the Palliative Care Team.
9.3  Hypocalcaemia

Check magnesium levels – if magnesium is low, this will need supplementing before the calcium will normalise. If calcium and magnesium are low and potassium is raised, consider EDTA (purple top tube) contamination – repeat sample, taking care to fill the SST (yellow top) tube before the EDTA one.

Calcium supplementation
- Add 3.5-7mmol (15-30mL calcium gluconate 10% injection) to 100mL sodium chloride 0.9% or glucose 5%
- Infuse over 30 minutes
- Repeat plasma calcium level
- Repeat dose as necessary
- Hypocalcaemic tetany: repeat dose until a response is achieved.
- ECG monitoring is recommended because dysrhythmias can occur if correction is too rapid.

9.4  Hyperkalaemia

- Identify and manage the underlying cause of hyperkalaemia.
  The emergency measures outlined below should be undertaken while treating the underlying cause or arranging a renal referral.
- Stop medicines that interfere with potassium excretion (e.g. angiotensin converting enzyme inhibitors, amiloride, spironolactone, NSAIDs)
- Management is guided by ECG changes. Generally, treatment is unnecessary if potassium concentration is less than 6.5mmol/L and there are no ECG changes.
  - If no p waves, broad QRS or worse
  1. Give IV calcium gluconate 10% immediately (10mL over 5 minutes is usually effective) ideally through wide bore venous access. Repeat until ECG returns to normal (up to 30mL may be required, and, in rare cases, up to 90mL has been necessary). This will not affect [K+] but will protect the myocardium until the potassium concentration is reduced. Calcium chloride contains approximately three times more calcium (6.8mmol/ 10mL) as compared with calcium gluconate (2.26mmol/ 10mL) per mL and is more likely to be effective after a single dose compared to calcium gluconate. It has thus been recommended in the setting of haemodynamic instability, including cardiac arrest. However, it is more of an irritant to veins.
  Caution with administration of intravenous calcium has historically been advised in patients with known or suspected digoxin toxicity. As hypercalcaemia may potentiate digoxin toxicity, a slower rate of administration, over 30 minutes, has been recommended in these patients.
  2. Give 10 units of soluble insulin over 30 minutes covered with 25g glucose IV which may be given as glucose 50% w/v (50mL over 30 minutes via a syringe driver) or as glucose 20% w/v (125mL over 30 minutes).
  This will reduce extracellular potassium concentration within about 30 minutes.
  The effect will last for 1-2 hours.
N.B.  25g glucose = 50mL glucose 50% w/v = 125mL glucose 20% w/v
Hypoglycaemia is the most common adverse reaction following insulin-glucose infusion for the treatment of hyperkalaemia, so monitor blood glucose regularly. High concentrations of glucose solutions are irritant to veins.

3. Start Calcium Resonium 15g 3-4 times a day PO, given in water. If patient is NBM it may be given rectally (30g, retained for 9 hours).
   If calcium is high, sodium-containing Resonium A may be given instead. Avoid Resonium A in CCF and renal impairment. Avoid Calcium Resonium in hyperparathyroidism, multiple myeloma, sarcoma or metastatic carcinoma.

4. Salbutamol 10-20mg via nebuliser can be used as adjuvant therapy for severe (K+ ≥ 6.5mmol/L) hyperkalaemia. (Caution – cardiovascular side effects and unlicensed indication – please discuss with senior colleague before prescribing.)
   N.B: Patients receiving non-selective beta-blockers are unlikely to manifest a hypokalaemic response to salbutamol. Up to 40% of patients with ESRD do not respond to salbutamol.

5. The aim of treatment is to achieve a serum K+ < 6.0mmol/L within 2 hours of initiation of treatment.

6. Discuss with the renal team if hyperkalaemia cannot be controlled (i.e. serum K+ persistently ≥ 6.5mmol/L) using medical measures, particularly if in the presence of advanced or oliguric renal failure (either AKI or CKD).

- If peaked T waves
  Give glucose and insulin as above.
  Calcium Resonium as above

- If potassium > 6.5mmol/L, no ECG changes
  Give Calcium Resonium as above. Review daily.

If the cause of hyperkalaemia is not readily apparent, contact the duty biochemist on Ext 48334/ UHW bleep 5452 for advice on further assessment and investigation.

9.5 Hypokalaemia

Measure magnesium if have not already done so – if low this will need supplementing before potassium will normalise. Consider checking calcium as low magnesium can cause hypocalcaemia as well as hypokalaemia.

The standard strength of potassium chloride available in ready mixed bags is 40mmol/L (available in glucose 5%, sodium chloride 0.9% and glucose 4%/ sodium chloride 0.18%).

WHEREVER POSSIBLE prescribe in 500mL or 1L volumes of fluid.
Generally, potassium concentrations in IV fluids should not exceed 40mmol/L; higher strengths become increasingly irritant to veins.

- Daily potassium requirement
  Daily potassium requirement is approximately 1-1.5mmol/kg/day to prevent hypokalaemia in patients who are nil by mouth (unless renal impairment present).

  Examples:
  to provide 80mmol potassium prescribe 2 x 1L of 40mmol/L potassium chloride
  (and if the patient needs 3L fluid: add 1 x 1L without potassium chloride)
  to provide 120mmol potassium prescribe 3 x 1L of 40mmol/L potassium chloride.
Nutrition and Blood

- **Rate of intravenous potassium administration**
  The rate of administration should not normally exceed 10mmol/hour. ECG monitoring is recommended for higher rates.

- **Potassium deficiency**
  When estimating potassium deficit, remember:
  - potassium is primarily intracellular and several factors can cause an extracellular-intracellular shift e.g. surgery, acidosis

  As a rule of thumb, a fall in plasma potassium of 0.27mmol/L equates to a deficit of 100mmol (up to a total of 500mmol). This may not need to be replaced over the next 24 hours. Consider the likely rate of potassium loss.

  If bicarbonate therapy is being used to treat hypokalaemic acidosis, the potassium stores should be replenished before bicarbonate is given because the latter will cause intracellular movement of potassium.

  Repeated measurements of plasma potassium are necessary to determine whether further infusions are required, and to avoid the development of hyperkalaemia: this is especially liable to occur in renal impairment.

9.6 **Hypophosphataemia**
Reference range, serum inorganic phosphate (0.8-1.45mmol/L)

Usual advice for symptomatic patients with hypophosphataemia needing intravenous administration (phosphate < 0.3mmol/L):
Before treatment, measure serum calcium, phosphate, urea, magnesium and creatine kinase. The decision to treat may depend on the cause. Use with caution in those with hypocalcaemia as serum calcium levels may decrease further as phosphate is replaced. These patients should ideally have their serum calcium corrected prior to replacing phosphate.

Add 1 x10mL vial (each 1mL contains 1mmol of potassium and 1mmol of phosphate) potassium acid phosphate (KH₂PO₄) to 500mL of sodium chloride 0.9% or glucose 5% and infuse over 12 hours.

A phosphate polyfusor containing 50mmol phosphate in 500mL can be administered over 12-24 hours (preferably 24 hours). This regimen is more often associated with severe hypocalcaemia and generally only advisable on an intensive care/high dependency unit. Calcium levels need to be monitored regularly during the infusion.

Table 2 gives some suggested doses of Phosphates Polyfusor based on weight for patients with normal renal function. Reduced doses may be necessary in patients with impaired renal function.
Table 2: Suggested doses of Phosphate Polyfusor (assuming normal renal function)

<table>
<thead>
<tr>
<th>Serum phosphate concentration</th>
<th>Weight 40 - 60kg</th>
<th>Weight 61 - 80kg</th>
<th>Weight 81 - 120kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amount of phosphate</td>
<td>Volume of polyfusor</td>
<td>Amount of phosphate</td>
</tr>
<tr>
<td>&lt; 0.3mmol/L</td>
<td>25mmol</td>
<td>250mL</td>
<td>35mmol</td>
</tr>
<tr>
<td>0.3-0.6mmol/L (if oral route not suitable)</td>
<td>10mmol</td>
<td>100mL</td>
<td>15mmol</td>
</tr>
</tbody>
</table>

The appropriate volume of Phosphate Polyfusor can be given over 6-12 hours but is commonly given over 12-24 hours. Repeated doses may be required on subsequent days.

Phosphate Polyfusors should be administered with caution to patients with cardiac failure, peripheral or pulmonary oedema, impaired renal function or conditions predisposing to hyperkalaemia due to the potassium and sodium content of Phosphates Polyfusors.

Treatment with potassium salts is contraindicated in the presence of hyperkalaemia or renal failure. In these cases, add 10mL (10mmol) sodium glycerophosphate 21.6% (1mmol phosphate and 2mmol sodium per mL, 20mL ampoule) to 500mL to 1L of sodium chloride 0.9% or glucose 5% and give over 12 hours.

- Reduce dose if potassium or phosphate rises above the reference range or if there is a significant fall in serum calcium.

Oral supplements:
Phosphate Sandoz (each tablet contains 16.1mmol phosphate, 3.1mmol potassium)
Dose 1-4 tablets daily. Review dose daily and adjust according to phosphate levels.
Oral phosphate supplements should not be taken with aluminium, calcium or magnesium salts as these will bind phosphate and reduce its absorption.

Adverse effects of phosphate therapy
Oral phosphate can cause diarrhoea and gastrointestinal upset. This is usually dose related and may be reduced by dividing the doses. Phosphate preparations are given as the potassium or sodium salts or both, and may be associated with hyperkalaemia, hypernatraemia and dehydration. Sodium phosphate may cause hypokalaemia. Management of adverse effects involves withdrawal of phosphate, general supportive measures, and correction of serum electrolyte concentrations, especially calcium. Measures to remove excess phosphate such as haemodialysis may sometimes be required.
Excessive doses of phosphates may cause hypocalcaemia and metastatic calcification. Reduce dose if potassium or phosphate rises above the reference range or if there is a significant fall in serum calcium.

For further advice contact your Ward Pharmacist or Medicines Information (Ext 42979 UHW or Ext 25262 UHL).

9.7 Hypomagnesaemia

- Clinical and biochemical manifestations of hypomagnesaemia include:
  - neuromuscular hyperactivity
  - psychiatric hypocalcaemia
  - hypokalaemia
  - ECG changes, supraventricular and ventricular arrhythmias
- Monitor blood pressure, respiratory rate, ECG, renal function, serum magnesium, potassium and calcium
- If calcium and magnesium are low and potassium unexpectedly high on the same sample, consider the possibility of EDTA contamination (purple top collection tube contents contaminating plasma or serum tubes during collection) – see entries for hypocalcaemia (section 9.3) and hyperkalaemia (section 9.4)
- IV therapy should be administered with caution in severe bradycardia, AV block, respiratory insufficiency and myasthenia gravis.

This is intended as general guidance. Protocols for coronary care, intensive care and other specialist areas may vary.

**Symptomatic hypomagnesaemia and/or serum magnesium <0.5mmol/L**

- The total body magnesium deficit, to produce symptoms and associated with significantly low plasma levels, is usually in the order of 0.5-1mmol/kg.

- The total amount to be given is therefore calculated from the patient’s body weight. Serum magnesium is a poor marker of total body magnesium. (please see table 3 on page 143).

- Some clinical judgement needs to be exercised when estimating the deficit taking into consideration the cause, ongoing losses etc. Twice the estimated deficit is given parentally as 50% of what is given will be excreted renally.

  50% Magnesium sulphate (0.5g/mL or 2mmol/mL) = 20mmol in 10mL

- Of the total amount to be given, 40mmol of magnesium is given over the first 24 hours. The rest is given as 20mmol daily for the following 3 to 5 days depending on the severity of the estimated deficit and the patient’s weight.

- Magnesium sulphate is typically added to 500mL or 1L of either sodium chloride 0.9% or dextrose 5%; clinical judgement should be exercised taking the patient’s fluid status into account. ECG monitoring is unlikely to be required.
with this regime unless there is specific clinical concern, such as cardiac instability in an older patient.

- Faster administration may be carried out safely, but the dose should not exceed 8mmol per hour and ECG monitoring is recommended.

- Slower replacement of magnesium is thought to result in improved retention of administered magnesium and apart from cardiac emergencies is therefore desirable for most clinical situations. The dose administered will need to be reduced in renal insufficiency.

**Monitoring serum magnesium during parenteral replacement is not helpful as serum concentrations will be spuriously high and are a poor indicator of treatment efficacy. A total weight adjusted dose should be administered as follows (estimate deficit of 0.5-1mmol/kg and multiply by 2 as assume 50% excreted renally following administration):**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Approximate amount of magnesium given over 3-5 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>50-100mmol</td>
</tr>
<tr>
<td>60</td>
<td>60-120mmol</td>
</tr>
<tr>
<td>70</td>
<td>70-140mmol</td>
</tr>
<tr>
<td>80</td>
<td>80-160mmol</td>
</tr>
<tr>
<td>90</td>
<td>90-180mmol</td>
</tr>
</tbody>
</table>

**Asymptomatic hypomagnesaemia or serum magnesium 0.5 - 0.7mmol/L**

- The oral route is preferred for treatment of asymptomatic or chronic magnesium deficiency. Parenteral therapy may be indicated in patients with poor gastrointestinal absorption, or who are intolerant of oral supplements.

- Approximately 20–50mmol per day given in divided doses may be required depending on the extent and route of losses.

- The tolerated dose is usually limited by diarrhoea.

Magnesium glycerophosphate 4mmol (1g) tablets are available (unlicensed):

- Two to four tablets per day in divided doses is usually sufficient in mild hypomagnesaemia

- Six to eight tablets per day in divided doses may be needed in more severe hypomagnesaemia titrated against side effects

- Magnesium glycerophosphate liquid is also available which contains 1mmol magnesium per mL.

There is some suggestion in the literature that some patients who are intolerant to magnesium glycerophosphate may tolerate another oral preparation, please contact the pharmacy regarding the availability of these.

Magnesium sulphate 4mmol in 500mL of compatible fluid has been administered subcutaneously over 6 to 12 hours overnight to successfully restore and maintain magnesium levels. Patients have been taught to self-administer this at home.
Nutrition and Blood

For all electrolyte abnormalities the cause should be elicited. For advice on investigating the cause contact the duty biochemist, UHW, Extension 48334, bleep 5452.
If the patient is on TPN the magnesium content can be adjusted - liaise with the nutrition team (see section 9.9).

9.8 Hyponatraemia

Hyponatraemia guidelines are available on the CAV UHB Clinical Portal.

9.9 Vitamin D deficiency

The diagnosis and management of vitamin D deficiency in children and adults guidelines (September 2013) are available on the clinical portal (under policies and procedures, then choose guidelines).

9.10 TPN and Nutrition Support Team

Referral or request for advice from UHB multi-disciplinary Nutrition Support Team (NST) may be made Monday-Friday between 8am and 5pm. Referrals for parenteral nutrition have to be received by 11am for same day compounding. PN is not available to be started at the weekend. The adult team is led by Dr A B Hawthorne (Consultant Gastroenterologist).

Contact numbers for Adult Nutrition Support Team (UHW and UHL):

<table>
<thead>
<tr>
<th>Role</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutrition Support Team office</td>
<td>Ext 46393</td>
</tr>
<tr>
<td>Lead Parenteral Nutrition Specialist Nurse</td>
<td>Suzanne Waldon-Smith Ext 46393</td>
</tr>
<tr>
<td>Parenteral Nutrition Nurse</td>
<td>Sian Tracey Ext 46393 Bleep 07623 906333</td>
</tr>
<tr>
<td>Dietitian Amelia Jukes</td>
<td>Ext 46393 Bleep 07623 905612</td>
</tr>
<tr>
<td>Pharmacists Susanna Harwood/Sophie Riddell</td>
<td>Ext 48639 Bleep 5646</td>
</tr>
<tr>
<td>Biochemist Dr Soha Zouwail</td>
<td>Ext 45448 Bleep 07623 906320</td>
</tr>
<tr>
<td>Gastroenterologist Dr Hawthorne</td>
<td>Ext 42183</td>
</tr>
<tr>
<td>Gastroenterologist Dr Durai</td>
<td>Ext 44572</td>
</tr>
<tr>
<td><strong>Enteral Nutrition Nurses</strong></td>
<td></td>
</tr>
<tr>
<td>Sarah Galliford, Ffion Jones, Mark Mapstone and Natalie Pinch</td>
<td>Ext 46393 Bleep 07623 905735 Ext 43144 Bleep 07623 905836</td>
</tr>
</tbody>
</table>

Contact numbers for Adult Nutrition Support Team (UHL):

<table>
<thead>
<tr>
<th>Role</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroenterologist Dr Swift</td>
<td>Ext 26812</td>
</tr>
<tr>
<td>Nutrition Nurse Natalie Pinch</td>
<td>Bleep 4463 Ext 25281</td>
</tr>
</tbody>
</table>
CHAPTER 10 MUSCULOSKELETAL AND JOINT DISEASES

10.1 NSAIDs (Non-steroidal anti-inflammatory drugs)

- Significant rate of minor side effects (e.g. dyspepsia) and a low rate of serious ones.
- Some patients may complain of wheezing or worsening of asthma.
- If symptoms are drug-related they will resolve quickly on stopping the NSAID.
- Side effects to one NSAID may not occur with other NSAIDs – if there is a clear indication for an NSAID and the side effect was minor, then an alternative NSAID may be prescribed.
- For patients with NSAID-induced dyspepsia, prescribe a proton pump inhibitor (PPI) (see section 1.3.2) or consider alternative treatments such as analgesics or a local steroid injection.
- Co-prescription of a PPI [e.g. omeprazole 20mg daily] should be considered as gastric protection if:
  - Using the maximum recommended dose of a NSAID
  - Aged 65 years or older
  - History of gastroduodenal ulcer, GI bleeding or gastroduodenal perforation.
  - Concomitant use of medications that are known to increase the likelihood of upper GI adverse events (e.g. anticoagulants, aspirin [even low dose], corticosteroids, and antidepressants [e.g. selective serotonin reuptake inhibitors, venlafaxine]).

- All standard NSAIDs (including the selective Cox-2 inhibitors - see section 10.2) can, to varying degrees, be associated with a small increased risk of thrombotic events. The lowest effective dose of NSAID should be prescribed for the shortest period of time to control symptoms and the need for long-term treatment should be reviewed periodically (see section 4.1 and 1.3.2).

10.2 Selective cyclo-oxygenase-2 (Cox-2) inhibitors

- Selective Cox-2 inhibitors are contra-indicated in ischaemic heart disease, cerebrovascular disease, peripheral arterial disease and mild to severe heart failure.

- Use second line in patients with inflammatory arthritis at high risk of developing gastro-intestinal complications following standard NSAID therapy (see risk factors below).

**Risk factors**

Age of 65 years and over.

Previous clinical history of gastro-duodenal ulcer, gastro-intestinal bleeding or gastro-duodenal perforation.

Concomitant use of medicines that increase the likelihood of upper gastro-intestinal adverse events e.g. steroids and anticoagulants.
Nutrition and Blood

Presence of cardiovascular disease, renal or hepatic impairment, diabetes or hypertension. Prolonged use of maximum recommended doses of standard NSAIDs

10.3 Disease modifying anti-rheumatic drugs (DMARDs) and NSAIDs

If these medicines have been discontinued during an in-patient stay consider whether they need to be restarted prior to hospital discharge.

- Flare ups of underlying rheumatic condition will occur if patients are discharged without their usual long term medication.
- Contact the Rheumatology SpR on call prior to discharge so that appropriate medication can be changed or restarted.
- If it is clear that the patient’s presenting complaint had nothing to do with the anti-rheumatic medication, then the original drug should be restarted prior to discharge.

10.4 Anti-TNF agents, rituximab, tocilizumab and abatacept

- The above biologic disease modifying agents are immunosuppressive and patients are at risk of developing infection. Patients admitted unwell on these agents should be screened for infection including atypical organisms.
- The treatment should be stopped if there is any suspicion of infection and the Rheumatology consultant looking after that patient and the anti-TNF Specialist nurse should be informed as soon as treatment is stopped for a plan to be in place for future treatment before the patient is discharged.

Please contact the Rheumatology SpR on call for advice about changes of treatment for Rheumatology patients.

10.5 Osteoarthritis

from NICE Clinical Guideline 59, February 2008 - Osteoarthritis

- Exercise - local muscle strengthening and general aerobic fitness
- Weight loss if overweight/obese.
- Consider transcutaneous electrical nerve stimulation (TENS) as adjunct.
- Arthroscopic lavage and debridement – only if patient has knee OA with a clear history of mechanical locking.
- Paracetamol 1g qds prn - regular dosing may be required
- Topical NSAIDS
- Topical capsaicin as adjunct for knee or hand osteoarthritis.
- Standard oral NSAID or a Cox-2 inhibitor (other than etoricoxib 60mg) plus a PPI
- Intra-articular corticosteroid injections as adjunct for relief of moderate to severe pain.

According to local expert opinion there is also an argument that intra-articular injection with steroid or hyaluronic acid and its derivatives are preferable to using oral NSAIDS if only one joint is symptomatic.
10.6 Polymyalgia rheumatica

- Prescribe prednisolone 15mg PO daily.
- If there is a good response to 15mg, reduce to 10mg daily after 4 weeks and slowly reduce thereafter according to symptoms.
- If there is not a rapid improvement using 15mg prednisolone daily, further investigations to exclude underlying disease (e.g. neoplasms) are required.

10.7 Temporal arteritis
(severe throbbing headache, scalp tenderness and jaw claudication)

- Urgent initiation of prednisolone 40-60mg po daily
- Refer to vascular surgeons for temporal artery biopsy
- Refer to Rheumatology outpatients for further management.
APPENDIX 1

Therapeutic Drug Monitoring (TDM) and Toxicology

Measuring blood concentrations of certain drugs with a narrow therapeutic range is useful for dose optimisation and for the detection of toxicity. Toxicological measurements (for overdose) are useful where specific therapeutic intervention is possible.

In order to obtain meaningful results, please:

a) take the blood sample at the correct time;

b) use the correct tube;

c) state the dosage, the time and date of the last dose and the time and date of blood sampling on the request form.

Samples analysed by Biochemistry Department, UHW (Ext 43560) and by Toxicology, Llandough Hospital (Ext 26894)

* Samples analysed at UHW only

** Samples analysed at Llandough only

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sample/Tube</th>
<th>Time</th>
<th>Therapeutic range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine**</td>
<td>Red min vol 0.5-1mL</td>
<td>Peak levels 2 hours post dose</td>
<td>5-20mg/L</td>
</tr>
<tr>
<td>Carbamazepine*</td>
<td>SST (yellow) min vol 1 mL</td>
<td>Immediately before next dose</td>
<td>4-10mg/L</td>
</tr>
<tr>
<td>Ciclosporin*</td>
<td>EDTA (lilac) min vol 0.5mL</td>
<td>Immediately before next dose</td>
<td>Renal transplants: First three months: 150-250 micrograms/L then 100-200 micrograms/L</td>
</tr>
<tr>
<td>Digoxin</td>
<td>SST (yellow) min vol 1mL</td>
<td>At least 6 hours after last oral dose 4 hours after IV</td>
<td>1.0-2.0 micrograms/L (normally 5 days to steady state)</td>
</tr>
<tr>
<td>Ethanol (Alcohol)</td>
<td>Fluoride Oxalate (grey) min vol 2mL</td>
<td>Not applicable</td>
<td>No “therapeutic” range. Legal driving limit &lt;800mg/L</td>
</tr>
<tr>
<td>Lithium</td>
<td>SST (yellow) min vol 1mL</td>
<td>12 hours after last dose</td>
<td>0.4-1.0mmol/L</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Li hep (green) min vol 1mL</td>
<td>At least 4 hours after overdose</td>
<td>Refer to nomogram for toxic levels</td>
</tr>
<tr>
<td>Phenytoin*</td>
<td>SST (yellow) min vol 1mL</td>
<td>Immediately before the dose</td>
<td>10-20mg/L</td>
</tr>
<tr>
<td>Salicylate</td>
<td>Li hep (green) min vol 1mL</td>
<td>If sample taken &lt; 6 hours after overdose and significant level present, repeat on another sample taken 3 hours later</td>
<td>“Therapeutic range” 150-300mg/L Toxic concentration &gt;350mg/L</td>
</tr>
</tbody>
</table>
### Appendix 1

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sample/Tube</th>
<th>Time</th>
<th>Therapeutic range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus*</td>
<td>EDTA (lilac) min vol 0.5mL</td>
<td>Immediately before next dose</td>
<td>Renal transplants 1st 3/12: 10-15 micrograms/L then 5-10 micrograms/L</td>
</tr>
<tr>
<td>Theophylline*</td>
<td>SST (yellow) min vol 1 mL</td>
<td>After oral dose: 2 hours (rapid release prep.) 4 hours (slow release prep.)</td>
<td>10-20mg/L (for adults)</td>
</tr>
<tr>
<td>Other drugs (for TDM) e.g. amiodarone</td>
<td>Clotted blood (red top tube)</td>
<td>Usually just before next dose</td>
<td>Contact Llandough Toxicology Department Ext 26894</td>
</tr>
</tbody>
</table>

Please contact Toxicology for information on any drug not listed in the above table - an extensive list of Toxicology/TDM assays is available on request. This information may also be obtained directly from [www.ctlabs.co.uk](http://www.ctlabs.co.uk).

Particular attention must be paid to sample collection, and although SST tubes may be used in some limited circumstances, they interfere with the vast majority of drug assays. If users of the service are unsure about the collection bottle to use they should err on the side of safety and opt for red topped tubes (i.e. plain).

For drugs of abuse (and for overdoses of uncertain cause where drug identification is important), also send 20mL random urine; these analyses are performed in the Llandough Hospital Toxicology Department.

It is recommended that most therapeutic drug ranges are now reported in mass units only ([Ann Clin Biochem 2002; 39:328-339](https://doi.org/10.1177/000456320203900303)).

### Samples analysed by Biochemistry Department UHW (Ext 43560)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sample/Tube</th>
<th>Time</th>
<th>Therapeutic range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin OD (once-daily dosing)</td>
<td>SST (Yellow) The request can be done by using the same tube used for requesting U&amp;Es (please refer to Lab Handbook on the intranet for further advice)</td>
<td>Refer to MicroGuide or seek advice from your ward pharmacist.</td>
<td>Refer to MicroGuide</td>
</tr>
<tr>
<td>Gentamicin MDD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
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<td></td>
<td></td>
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<tr>
<td>Chloramphenicol</td>
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<td>Fluconazole</td>
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<td>Fluycytosine</td>
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<tr>
<td>Netilmicin</td>
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<td>Co-trimoxazole</td>
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<tr>
<td>Teicoplanin</td>
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<td></td>
<td></td>
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<tr>
<td>Tobramycin</td>
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</table>

Some of these tests might be analysed off site.

Refer to [MicroGuide](http://www.ctlabs.co.uk) or refer to:
- Microbiology for advice (Ext 44825 or 42718)
- Medicines Information (Ext 42979 UHW or Ext 25262 Llandough)
Appendix 1

Assay Availability
The Assays will be available routinely 7 days a week between 9am and 6pm and are processed at UHW, outside of these hours requests will only be processed if approved by a Medical Microbiology Clinician.

All requests are treated as routine and no accelerated service is available with samples being processed in a timely fashion during the period outlined above. On Monday-Friday between 9am and 6pm and Saturday and Sunday morning, samples are run in real time while on Saturday and Sunday afternoon (post 12:15pm) a single run is performed around 6pm.

DOSE TO BE GIVEN (DO NOT WAIT FOR LEVEL RESULT if normal renal function), modifications to be made to next dose if required (please refer to MicroGuide)

Please Note: There is no routine transportation of Biochemistry samples from UHL to UHW after 3pm on Friday until 9am on Monday, for any requests during this period wards/units will need to arrange transportation to UHW.
APPENDIX 2

Policy on Writing Prescriptions

The purpose of this policy is to support safe, accurate prescribing and administration of medicines, dressings and intravenous fluids to patients.

Prescribers (medical or non-medical) will be required to comply with the UHB’s policies and procedures which relate to prescribing. When more than one significant incident or frequent minor contraventions of the policy which are attributable to an individual doctor, nurse or pharmacist are identified, the appropriate clinical Consultant or, if necessary, the appropriate Clinical Director, will be informed. Further incidents relating to that individual within 6 months will be reported to the appropriate Clinical Director and Associate Medical Director.

1. The minimum details required before inpatient, discharge or outpatient prescriptions will be dispensed are: name, address, date of birth and hospital number (on addressograph) and the weight for children under 12 years.

2. It is the responsibility of the prescriber to ensure that all charts have the patient’s details entered in full.

3. All handwriting for purpose of prescribing must be neat and clearly legible. Capital letters are preferable. English must be used. Indelible (blue or black) ink must be used (not a fountain or felt pen – these smudge if the chart becomes wet).

4. Abbreviations of drug names must not be used. Approved names should be employed at all times, although there are occasions when the brand name may need to be specified. Particular care must be exercised when prescribing compound preparations.

5. All prescriptions must be signed and dated at the time of writing.

6. Numbers for dosages should be clear and unambiguous.

7. Units e.g. milligrams (mg) should be clearly defined. In the case of micrograms or nanograms, this must be written in full (ug or ng are not acceptable).

8. Decimal points must not be employed unless essential. If the use is considered necessary, the decimal point must be precisely marked, and if appropriate preceded by a zero (0), e.g. 0.5mL NOT .5mL

9. In the case of drugs where the dose is prescribed in units, e.g. heparin or insulin, the dose must be prescribed as UNITS not u. Special care must be taken to ensure that the U in UNITS does not look like a zero (0).
10. When prescribing a liquid preparation (injection, oral mixture etc), the dose must be in **milligrams / micrograms / nanograms NOT mLs**, unless it is unavoidable to use a volume.

**In-patient prescriptions**

1. Regular prescriptions can be changed ONCE (dose, frequency or route) – enter the date of change and initials.

2. When drugs are prescribed “as required/PRN” the prescription must include the reason for the drug to be administered, the interval between doses and the maximum dose in 24 hours.

3. Whenever possible only ONE prescription chart should be in use for a patient. Where more than ONE chart is necessary, each chart must be clearly labelled chart 1 of 2, chart 2 of 2 etc, as appropriate. Charts must be regularly reviewed to condense to a minimum number of charts on a regular basis. Continuation sheets for administration records **must not be used**.

4. When an in-patient chart is rewritten, ensure all relevant information is transcribed on the new chart (e.g. allergies). The start date for a drug is the ORIGINAL start date, not the date that the chart is rewritten.

5. Prescription charts should be regularly reviewed for tidiness and legibility. Charts must be rewritten whenever legibility of a drug chart is compromised e.g. something spilled on the chart, where two charts are in use due to cancellations but currently therapy would fit on one chart.

6. When a supplementary chart is used (steroid, anticoagulant, insulin etc.) the drug must be identified on the main prescription chart and annotated “see accompanying chart”.

7. On discontinuation of a prescribed drug, the “crossing off” should occur through the prescribing section of the chart (i.e. the boxes containing the name of the drug, dose, frequency etc.) and through the section of the chart used to record administration of the drug.

8. Further details on how to use the UHB drug chart(s) are available, contact your ward or directorate pharmacist.
APPENDIX 3

Controlled Drugs: Writing Discharge Prescriptions

- WRITE the whole prescription (including patient’s name and address) in indelible ink in your own handwriting. (Do not use addressographs).

- State the:
  
  Drug Name  
  Drug Form  
  Dose  
  Frequency  
  Drug Strength to be supplied  
  Total Quantity to be supplied IN WORDS AND FIGURES

  e.g. For a patient receiving Oramorph 5mg q4h PRN, write:
  Oramorph solution 10mg in 5mL
  2.5mL 4-hourly  PRN 100 (one hundred) mL

  e.g. For a patient receiving MST 20mg bd for 1 week, write:
  MST tablets 20mg bd 28 (twenty-eight) 10mg tablets

N.B. If a patient is receiving a combination of strengths of one drug the total quantity of each strength should be written:

  e.g. MST tablets 40mg bd 14 (fourteen) 30mg tablets
       14 (fourteen) 10mg tablets

For injections the total number of ampoules to supply should be stated:

  e.g. For a patient receiving diamorphine 40mg over 24 hours via syringe driver:
       Diamorphine injection 40mg over 24 hours via SC syringe driver

       Supply 7 (seven) 30mg ampoules
       7 (seven) 10mg ampoules

- Sign AND date the prescription.
APPENDIX 4

**Clinical Nurse Specialists**

**University Hospital of Wales (UHW)**

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<thead>
<tr>
<th>Speciality</th>
<th>Contact No</th>
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<tbody>
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<td>Cardiac Rehabilitation</td>
<td>Ext 43384</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Ext 43350</td>
</tr>
<tr>
<td>Dermatology</td>
<td>Ext 46679 / 43278</td>
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<tr>
<td>Diabetes</td>
<td>Ext 42407</td>
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<tr>
<td>Endocrinology</td>
<td>Ext 43495</td>
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<tr>
<td>Epilepsy</td>
<td>Ext 45066</td>
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<tr>
<td>Haemophilia Centre</td>
<td>Ext 43403</td>
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<tr>
<td>Hepatobiliary</td>
<td>Bleep 5862</td>
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<tr>
<td>Infection Control</td>
<td>Ext 42165 / 48734</td>
</tr>
<tr>
<td>Nutrition Nurse</td>
<td>Ext 46393</td>
</tr>
<tr>
<td>Occupational Health</td>
<td>Ext 44265</td>
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<tr>
<td>Paediatric Diabetes</td>
<td>Ext 45435</td>
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<tr>
<td>Paediatric Growth</td>
<td>Ext 43478</td>
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<tr>
<td>Pain Control</td>
<td>Ext 45449 / Bleep 5414</td>
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<tr>
<td>Palliative Care/MacMillan</td>
<td>Ext 43377</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>(01778) 3838</td>
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<tr>
<td>Rheumatology</td>
<td>Ext 48191</td>
</tr>
<tr>
<td>Smoking Cessation nurse</td>
<td>Ext 43582</td>
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<tr>
<td>Drug and Alcohol</td>
<td>Ext 44901</td>
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<tr>
<td>Upper GI</td>
<td>Bleep 6578</td>
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<tr>
<td>Urology Cancer</td>
<td>Ext 48401</td>
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<tr>
<td>Vascular</td>
<td>Ext 42699</td>
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<tr>
<td>Wound Healing</td>
<td>Ext 46506</td>
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## University Hospital Llandough (UHL)

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</tr>
<tr>
<td>Breast Care</td>
<td>Ext 25058</td>
</tr>
<tr>
<td>Community Respiratory Resource</td>
<td>Ext 25237 / 25092</td>
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<tr>
<td>Cystic Fibrosis</td>
<td>Ext 25465</td>
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<tr>
<td>Diabetes</td>
<td>Ext 25651</td>
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<tr>
<td>Infection Control</td>
<td>Ext 25512</td>
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<td>Interstitial Lung Disease</td>
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<tr>
<td>Lung Cancer</td>
<td>Ext 25642</td>
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<td>Nutrition Support</td>
<td>Ext 25634</td>
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<td>Respiratory Medicine</td>
<td>Ext 26851</td>
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<td>Tuberculosis, TB Control</td>
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<td>Lipid Control (Apheresis)</td>
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<td>Pain Control</td>
<td>Ext 25020 / Bleep 560</td>
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</table>

District Nursing Contact Centre 029 2044 4501 (24-hour service)
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