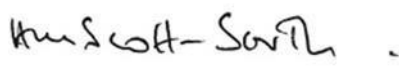


## MANAGEMENT OF MEDICATION IN THE PERI-OPERATIVE PERIOD

Approved by:	Trust Executive Committee
On:	January 2018
Review Date:	January 2020 – <b>Ext to April 2024</b>
Corporate / Divisional	Divisional
Clinical / Non Clinical	Clinical
Department Responsible for Review:	Pre-Assessment Clinic / Pharmacy Department
Distribution:	Pre-Assessment Nursing Staff
<ul style="list-style-type: none"><li>Essential Reading for:</li><li>Information for:</li></ul>	<b>Anaesthetists Clinical theatre Manager Theatres Operational Manager Surgeons Pharmacists</b>
Policy Number:	353
Version Number:	1
Signature:	
	Chief Executive
Date :	30 January 2018

# Burton Hospitals NHS Foundation Trust

## POLICY INDEX SHEET

<b>Title:</b>	<b>Management of medication in the peri-operative period</b>
<b>Original Issue Date:</b>	<b>January 2018</b>
<b>Date of Last Review:</b>	<b>New policy</b>
<b>Responsibility:</b>	<b>Matron for pre-assessment nursing Principal Pharmacist for Surgery</b>
<b>Stored:</b>	<b>Intranet</b>
<b>Key words:</b>	<b>Peri-operative medication Anticoagulation</b>
<b>Linked Trust Policies:</b>	<b>Pre-assessment Clinical Operational Policy Warfarin Policy VTE thromboprophylaxis policy Perioperative diabetes guidelines</b>
<b>Equality Impact Assessed</b>	
<b>Consulted</b>	<b>Head of Pharmacy Clinical Director for Anaesthetics Clinical Director for Surgery Consultant Haematologist Consultant Cardiologist Consultant Rheumatologist</b>

# Burton Hospitals NHS Foundation Trust

## REVIEW AND AMENDMENT LOG

Version	Type of change	Date	Description of Change
1		January 2018	New Policy

# Burton Hospitals NHS Foundation Trust

## CONTENTS

Paragraph Number	Subject	Page No.
1	Scope	1
2	Introduction	1
3	Anticoagulation	<b>1 - 8</b>
3.1	Assessment of Requirements	1 - 2
3.2	Low risk Patients	3 - 4
3.3	Intermediate risk patients	4 - 5
3.4	High Risk Patients	5 - 6
3.5	Emergency Surgery	6 - 8
4	Antiplatelets	<b>8 - 9</b>
5	Diabetes treatments	<b>9</b>
6	Cardiovascular medications	<b>9 - 11</b>
6.1	ACE inhibitors and Angiotensin receptor blockers	9 - 10
6.2	Dihydropyridine Calcium Channel Blockers	10
6.3	Statins	11
7	Rheumatology/ immunosuppressant drugs	<b>11 - 13</b>
8	Centrally acting drugs	<b>13 - 17</b>
8.1	Opioids	13 – 14
8.2	Antiepileptic drugs	15
8.3	Antiparkinsons medication	15 - 16
8.4	Antidepressants	16 - 17
9	Hormonal therapies	<b>17 - 18</b>
9.1	Tamoxifen and Raloxifene	17
9.2	Hormone Replacement therapy	18
9.3	Combined oral contraception	18
9.4	Progesterone only contraception	18
10	References	<b>19</b>

Appendix A	Calculation of CHA <sub>2</sub> DS <sub>2</sub> VASc	20
Appendix B	Prophylactic doses of Enoxaparin	21
Appendix C	Treatment doses of Enoxaparin in High thromboembolic risk patients with metallic heart valves	22
Appendix D	Treatment doses of Enoxaparin in other High thromboembolic risk patients	23
Appendix E	Antiplatelet flow chart	24

## MANAGEMENT OF MEDICATION IN THE PERI-OPERATIVE PERIOD

### 1. SCOPE

The aim of this Policy is to support the decisions required around the management of medications in the peri-operative period.

This Policy covers a range of drug groups that need to be considered in patients undergoing elective surgery at Burton Hospitals NHS Foundation Trust (the Trust).

### 2. INTRODUCTION

Patients undergoing elective surgery who are taking regular medications may require adjustments to these medications prior to surgery, and in the immediate period around their procedure.

It is essential that these adjustments are made consistently and safely, to prevent harm to these patients and / or cancellation of their planned surgery. This is particularly important with anticoagulant medications, due to the high risks associated with these.

The following sections cover some of the major groups of medications that need to be considered during the peri-operative period.

### 3. ANTICOAGULATION

#### 3.1 Assessment of requirements

Management of anticoagulation (with Warfarin and other coumarin anticoagulants and DOACS (Apixaban, Rivaroxaban and dabigatran)) in the peri-operative period requires special care.

***The Pre-operative nurse should assess the following, with input where required from the patients surgical or medical team.***

- Assess the thrombosis risk for the patient using the following guidance*
- *Assess the need to 'bridge' any interruption with Enoxaparin according to the patient's thrombosis risk - if in doubt, seek advice from haematology and/or the relevant medical /surgical team*
- Arrange for a supply of Enoxaparin for patients requiring bridging therapy to be issued by the hospital pharmacy. GPs SHOULD NOT BE ASKED TO PRESCRIBE BRIDGING THERAPY*
- Remember:*** *Cancellation of surgery or an elective procedure for patients on warfarin will either lead to an increased period of bridging (even if warfarin is restarted) or the potential for patients to receive inadequate or no anticoagulation putting them at increased risk of thrombotic events. Where cancellation is unavoidable, contact the pre-assessment unit or the responsible medical or surgical team for further advice*

The following should be considered in all patients undergoing elective surgical procedures;

- i. The risk of bleeding from the procedure
  - ii. The risk to the patient of not being anti-coagulated.
- i. The risk of bleeding from the procedure  
Unless advised by the consultant prior to the pre-op appointment, all procedures should be considered to carry a bleeding risk that requires adjustment of a patients anti-coagulation.  
All patients taking anti-coagulants, therefore require assessing for their risk of thrombosis.
  - ii. The risk to the patient of not being anti-coagulated  
The risk of thrombosis depends on the indication for anticoagulant therapy. Patients can be classified as Low, Intermediate or High risk. The following table clarifies these groups:

\*For calculation of CHA<sub>2</sub>DS<sub>2</sub>VASc, see appendix A.

Once the thrombosis risk has been calculated the guidance below needs to be followed:

Thrombosis Risk	Indication for Anticoagulant Therapy		
	Mechanical Heart Valve (MVR)	Atrial Fibrillation	VTE
<b>LOW</b>	Tissue valve replacement with no AF or TIA/CVA	CHA <sub>2</sub> DS <sub>2</sub> VASc score 0-4 with <i>no</i> history of CVA/TIA in the last 3/12	Single VTE more than 12 months ago
<b>INTERMEDIATE</b>	Bi leaflet mechanical aortic valve replacement		VTE occurring between 12 weeks and 12 months ago; <ul style="list-style-type: none"> <li>- Single VTE</li> <li>- Recurrent VTE occurring <i>off</i> anticoagulation</li> <li>- VTE associated with active cancer</li> </ul>
<b>HIGH</b>	Mechanical Valve replacement (patient <b>WILL</b> be on warfarin) – except bi-leaflet aortic valves with no other complications	CHA <sub>2</sub> DS <sub>2</sub> VASc* score 5 or more <i>or</i> history of CVA/TIA in the last 3/12	VTE within last 12 weeks (avoid surgery if possible) – seek haematology advice Recurrent VTE occurring <i>on</i> anticoagulation – seek haematology advice Severe thrombophilia disorder – seek haematology advice Any indication with target INR 3-4

## 3.2 Low thromboembolic risk patients

Patients with a low thrombosis risk DO NOT require any type of bridging therapy during the pre-operative period. Management of their anticoagulant therapy depends on the drug being taken and their renal function.

### 3.2.1 Patients on Warfarin

- Warfarin should be stopped 5 days prior to the planned surgery. An INR should be checked on the morning of the planned surgery and if necessary oral vitamin K administered
- Following surgery, prophylactic Enoxaparin should be administered as per the Trust policy on VTE thromboprophylaxis ([Venous Thrombo-embolism \(VTE\) Risk Assessment, Thromboprophylaxis and Management in Adult inpatients aged 16 years and over - Trust Policy and Procedure - Burton Sites Only](#)) and warfarin should be restarted at the patients usual dose when the patient is able to tolerate oral medications and take a light diet (loading doses are not required)
- The patients INR should be monitored every day, once warfarin has been restarted and prophylactic Enoxaparin administered until the INR is within the patients usual target range, or discharge
- At discharge, ensure that the patient has an appointment for INR follow up at their usual anticoagulation clinic within 3 – 5 days of discharge, and complete a warfarin discharge form for all patients.

### 3.2.2 Patients on DOACS

- The DOACS (Apixaban, Rivaroxaban and Dabigatran) have a shorter half-life than warfarin, and the length of time they require stopping for prior to a surgical procedure varies with the drug being taken and the patients renal function
- Due to the shorter half-life, they also have a faster onset of action. Following surgery, the timing of restarting is at the discretion of the surgeon. In the interim, patients should receive VTE prophylaxis as per the Trust policy. Once their usual anticoagulation is restarted, they do NOT require VTE prophylaxis with LMWH (Enoxaparin)
- The following table summarises the requirements for each DOAC. This has been adapted from the British Society of Haematologists guidelines 2016:

Drug	Renal Function (CrCl ml/min)*	Estimated half life (hours)	Last dose of DOAC (pre-surgery)
Dabigatran	>80	13	2 days
	>50 to <80**	15	3 days
	>30 to <50**	18	4 days
Rivaroxaban	>30	9	2 days
	<30**	9	3 days
Apixaban	>30	8	2 days



	<30**	8	3 days
<b>Edoxaban</b>	>30	10 - 14	2 days
	<30**	10 - 14	3 days

\*Renal function should be calculated as estimated Creatinine Clearance using the Cockcroft-Gault equation– eGFR should NOT be used. For calculation of estimated creatinine clearance see appendix A

\*\* Patients with Chronic renal impairment (CKD) and historical blood results in these categories, may be referred to a consultant.

### 3.3 **Intermediate thromboembolic risk patients**

Patients who have an intermediate risk of thrombosis usually require therapy with a prophylactic dose of LMWH (Enoxaparin) in the period around surgery. As above, the management of these patients depends on the anticoagulant they are taking and their renal function.

#### 3.3.1 **Patients on Warfarin**

- Warfarin should be stopped 5 days before the planned procedure
- Patients should start prophylactic Enoxaparin (adjusted according to body weight – see appendix B) from day 3 prior to the planned procedure. This should be administered each morning
- The last dose should be given on the morning before the procedure
- Enoxaparin should not be given on the morning of the procedure
- Prophylactic Enoxaparin should be administered on the evening of the surgery, when haemostasis is secure, based on the advice of the anaesthetist in charge of the patient
- Patients requiring spinal anaesthesia or at high risk of bleeding, may have this delayed at the discretion of the surgeon or anaesthetist responsible for the patient
- Warfarin should be restarted at the patients usual dose when the patient is able to tolerate oral medication (loading doses are not required). Prophylactic Enoxaparin should be continued until the INR is within its usual range. Once warfarin is restarted, the INR should be checked daily until discharge
- On discharge, ensure that the patient has an appointment for INR follow up at their usual anticoagulation clinic within 3 – 5 days of discharge, and complete a warfarin discharge form for all patients.

#### 3.3.2 **Patients on DOAC**

- The patient should be advised to stop their DOAC as per the table above for low thromboembolic risk patients (Section 3.2.2)

- They should receive prophylactic Enoxaparin (adjusted according to body weight – see appendix B) from the following morning until the day before the proposed surgery
- Enoxaparin should not be given on the morning of the procedure
- Prophylactic Enoxaparin should be administered on the evening of the surgery, when haemostasis is secure, based on the advice of the anaesthetist in charge of the patient
- Due to the shorter half-life, they also have a faster onset of action. Following surgery, the timing of restarting is at the discretion of the surgeon. In the interim, patients should receive VTE prophylaxis as per the Trust policy. Once their usual anticoagulation is restarted, they do NOT require VTE prophylaxis with LMWH (Enoxaparin).

### 3.4 **High thromboembolic risk patients**

Patients at high risk of thromboembolic events require bridging with a dose of LMWH (Enoxaparin) closer to therapeutic treatment doses in the period around surgery. As above, the management of these patients depends on the anticoagulant they are taking and their renal function.

#### 3.4.1 **Patients on Warfarin**

- Warfarin should be stopped 5 days before the planned procedure
- Patients should start treatment dose Enoxaparin (see appendix C for patients with metal heart valves, and appendix D for other high risk patients) from day 3 prior to the planned procedure. The dose is dependent on the patients weight AND the reason for anticoagulation
- The last dose should be given on the evening before the procedure, allowing for at least 12 hours before the planned procedure
- Enoxaparin should not be given on the morning of the procedure
- Prophylactic Enoxaparin should be administered on the evening of the surgery, when haemostasis is secure, based on the advice of the anaesthetist in charge of the patient
- Patients requiring spinal anaesthesia or at high risk of bleeding, may have this delayed at the discretion of the surgeon or anaesthetist responsible for the patient
- Treatment dose Enoxaparin should be restarted the day following surgery, assuming haemostasis is secure. For high bleeding risk patients, this may be delayed for up to 48 hours at the discretion of the surgeon
- Warfarin should be restarted at the patients usual dose when the patient is able to tolerate oral medication (loading doses are not required). Treatment dose Enoxaparin should be continued until the INR is within its usual range. Once restarted, the INR should be checked daily until discharge

- On discharge, ensure that the patient has an appointment for INR follow up at their usual anticoagulation clinic within 3 – 5 days of discharge, and complete a warfarin discharge form for all patients.

### 3.4.2 Patients on DOACS

- The patient should be advised to stop their DOAC as per the table above for low thromboembolic risk patients (Section 3.2.2)
- They should receive treatment dose Enoxaparin (see Appendix C and D) from the following morning until the day before the proposed surgery
- Enoxaparin should not be given on the morning of the procedure
- Prophylactic Enoxaparin should be administered on the evening of the surgery, when haemostasis is secure, based on the advice of the anaesthetist in charge of the patient
- Due to the shorter half-life, they also have a faster onset of action. Following surgery, the timing of restarting is at the discretion of the surgeon. In the interim, patients should receive treatment dose LMWH as per these guidelines. Once their usual anti-coagulation is restarted, they do NOT require further LMWH (Enoxaparin).

### **Guidelines for ALL patients**

1. Although it is accepted national and international practice, bridging therapy is an unlicensed use of Enoxaparin. Patients should be informed and their consent gained, which can be documented in the notes or clinic letter for all patients. This consent can be verbal, but MUST be documented.
2. In all warfarin patients, INR should be checked on the morning of surgery to allow for correction if needed.
3. Routine platelet monitoring is not usually required, unless there is evidence of bleeding or the patient is septic. All patients on anticoagulation, should have a baseline FBC, U&E, LFT's checked and reviewed on admission.
4. Administration of Enoxaparin is not recommended whilst an epidural catheter is in situ. Placement or removal of a catheter for epidural or spinal anaesthesia must be delayed at least 24 hours after the last administered therapeutic dose, or at least 12 hours after the last administered prophylactic dose of Enoxaparin. In all such patients, therapy should be discussed with the anaesthetist in charge of the patient.

### 3.5 **Emergency Surgery**

If patients currently taking anticoagulants (coumarins and DOACS) require urgent / emergency surgery, the following guidance should be followed:

### 3.5.1 Patients on Warfarin

The action required is dependent on whether surgery can be delayed for 6-8 hours:

- If the surgery can be delayed for 6 – 8 hours, then 5 mg Intravenous phytomenadione should restore coagulation factors. INR should be checked after 6-8 hours
- If surgery is required more urgently, anticoagulation can be reversed with prothrombin complex concentrate (PCC) – Please discuss individual cases with the on-call consultant haematologist. When PCC is used, Vitamin K administration, at the same time as the administration of PCC, is essential in all patients
- Post-operatively, patients should be managed as in sections 3.2, 3.3 or 3.4 depending on their thrombosis risk.

### 3.5.2 Patients on DOAC

The half-life of DOACs is shorter than warfarin (see table in section 3.2.2). Where possible, surgery should be delayed to allow the anticoagulant effect to wear off. The concentration can be approximated by considering the timing of the last dose and other patient factors (age, weight, renal function etc)

Routine coagulation tests can give a guide to the drug levels and degree of anticoagulation, but they do not give an exact measure of the anticoagulation levels in patients on DOACs. PT and APTT measurements should be discussed for individual cases with the on-call consultant haematologist.

If surgery is essential, the following can be considered:

- Tranexamic acid is likely to reduce bleeding in patients who have a residual anticoagulant effect
- Prothrombin Complex concentrates should not be routinely used in patients on DOACS. Individual cases should be discussed with the on-call consultant haematologist
- Specific Reversal Agents

#### Idarucizumab

Idarucizumab is a monoclonal antibody that is a specific reversal agent for Dabigatran. There is a limited supply of this drug available in the Trust. All usage should be discussed with the on-call consultant Haematologist.

<http://bhftintranet.burtonft.nhs.uk/Departments/pharmacy/prescribing%20tips%20page/Dabigatran%20reversal%20protocol%20draft%202%20dec%202016.pdf>

#### Adexanet

Adexanet is a reversal agent that is currently undergoing trials for the reversal of Rivaroxaban and Apixaban. It is not yet available (2017) for use, and had not yet been studied in patients undergoing emergency surgery. It

is unlikely to be available in the near future. Use of this drug will be directed by the consultant Haematologists.

As with warfarin, post-operatively, patients should be managed as in Sections 3.2, 3.3 and 3.4 depending on their thrombosis risk.

#### 4. ANTIPLATELETS

Antiplatelet drugs (aspirin, clopidogrel, prasurgel and ticagrelor) are prescribed for either primary (aspirin or clopidogrel) or secondary (all drugs) prevention of cardiovascular disease. The action required depends on the indication.

##### **Primary Prevention**

Patients on antiplatelet drugs for primary prevention are thought to be at risk of heart attack or stroke, but have not had one.

For these patients the following applies:

**Aspirin** - this can safely be continued unless the surgeon deems there is an unacceptable bleeding risk. In these cases, Aspirin should be stopped 3 – 5 days before the procedure.

**Clopidogrel** – this should be stopped 7 days prior to the procedure.

##### **Secondary Prevention**

Patients on antiplatelet drugs for secondary prevention have significant cardiovascular disease.

This includes patients with previous Heart attack, Angioplasty or coronary artery stents, Angina, Stroke, Peripheral Vascular disease and renovascular disease.

The action required in these patients, depends on the indication.

Secondary prevention patients being treated for coronary artery disease may be on Clopidogrel or Prasurgel or Ticagrelor (C,P,T) in addition to aspirin.

**Aspirin** – As with primary prevention, this can be safely continued unless otherwise advised by the surgeon (see primary prevention).

**Clopidogrel, Ticagrelor and Prasurgel** – These drugs are usually given in combination with aspirin for a fixed period following a cardiovascular event (secondary prevention), or procedure (PCI):

- Following a cardiovascular event

Unstable Angina and post infarct – consult Cardiologist if within 12 months

- Continue C,P or T for 3 months minimum
  - Avoid surgery during this time if possible
  - C,P or T, may be continued for up to 12 months
  - Surgery can be considered in the second 6 months.
- Following PCI (stenting)

Patients are usually on dual antiplatelet therapy to prevent re-occlusion of the stent that has been inserted. The usual duration is for 12 months.

All patients who have had a Cardiac stent inserted in the last 12 months should be referred back to their Cardiologist for an opinion on the antiplatelet therapy. The risk varies, depending on the type of stent used, so advice should always be sought.

Stopping anti-platelet medication before endothelialisation of the stent has occurred increases the risk of myocardial infarction with a high mortality for the patient.

Ideally in patients with a recent incidence of ACS, or recent PCI, surgery should be delayed until dual anti-platelet therapy can be safely discontinued.

- Stroke/TIA patients

Patients who have recently had a stroke, are at high risk of further stroke if their antiplatelet medication is stopped. All surgery should be avoided for a minimum of 6 weeks following a stroke or TIA. Ideally, elective surgery should not take place for 3 months.

After 3 months, the clopidogrel should be stopped for 7 days pre-operatively and 7 days post-operatively. During this period, aspirin 75mg should be given unless contraindicated as above.

If surgery is required urgently prior 3 months post stroke, consult the physician responsible for the patients care.

Note, minor procedures such as CT guided biopsies should be possible within shorter timescales following discussion with the relevant physicians.

See Appendix E for a flowchart summarising the above.

## 5. DIABETIC PATIENTS

Please refer to the Perioperative diabetes guidelines: <https://derby.koha-ptfs.co.uk/cgi-bin/koha/opac-detail.pl?biblionumber=2914>

## 6. CARDIOVASCULAR MEDICATIONS

### 6.1 ACE inhibitors and Angiotensin receptor blockers

ACE inhibitors and angiotensin receptor blockers are used in the treatment of hypertension, heart failure and following an MI as secondary prevention. Drugs in this group include:

### ACE inhibitors

- Captopril
- Cilazapril
- Enalapril
- Fosinopril
- Imidipril
- Lisinopril
- Moexipril
- Perindopril
- Quinapril
- Ramipril
- Trandolapril

### Angiotensin receptor blockers

- Candesartan
- Eprosartan
- Irbesartan
- Losartan
- Olmesartan
- Telmisartan
- Valsartan

### Risks

- If given prior to surgery, there is a risk of the patient experiencing hypotension.

### Advice

- Withhold on the day of surgery for all patients being treated for hypertension or post MI.
- Take as usual for patients being treated for documented heart failure (CCF, HF, LVF).

## **6.2 Dihydropyridine Calcium Channel Blockers**

Drugs in this group include:

- Amlodipine
- Felodipine
- Nifedipine
- Lacidipine
- Lercanidipine
- Nicardipine

### Risks

- The risks of continuing the drugs include an enhanced additive hypotensive effect due to the antihypertensive agent being given with anaesthetics such as enflurane and isoflurane
- The risk from stopping the drugs are a rebound hypertension and coronary vasospasm leading to an exacerbation of angina.

### Advice

- These medications should be continued in the peri-operative period.

### 6.3 **Statins**

Drugs in this group include:

- Atorvastatin
- Fluvastatin
- Pravastatin
- Rosuvastatin
- Simvastatin

#### Risks

- There is no evidence that statins can increase the risk of myopathy following major vascular surgery
- There is some evidence that statin discontinuation is associated with an increased risk for post-operative troponin release, myocardial infarction and cardiovascular death, compared with statin continuation in long term users.

#### Advice

- Statin therapy should be continued during the peri-operative period.

## 7. **RHEUMATOLOGY / IMMUNOSUPPRESSANT DRUGS**

This section covers a large number of drugs that have an effect on the immune system. They can be used in a number of conditions including:

- Rheumatology
- Dermatology
- Gastroenterology
- Immunosuppression following transplant
- Haematology

Drugs in this group include:

- Azathioprine
- Ciclosporin
- Hydroxychloroquine
- Mercaptopurine
- Methotrexate
- Mycophenolate
- Biological agents (e.g. Infliximab, adalimumab)

The following factors need to be considered:

- For all patients who have undergone organ transplant and are taking immunosuppressant drugs, the advice of the Consultant responsible for the patients care relating to their transplant should be sought
- For haematology patients, advice should be sought from the consultant responsible for the patients care



- For all other conditions discuss with the consultant responsible for the patients care.

The table below summarises the information relating to each drug that is available in reference sources. The final decision on treatment should be that of the Consultant:

<b>Drug</b>	<b>Indications</b>	<b>Risks associated with surgery</b>	<b>Advice</b>
<b>Azathioprine</b>	<ul style="list-style-type: none"> <li>• Immunosuppressive regimes</li> <li>• Prophylaxis of transplant rejection</li> <li>• Rheumatology conditions</li> <li>• Inflammatory bowel disease</li> <li>• Haematology conditions</li> </ul>	<p>The following have been identified:</p> <ul style="list-style-type: none"> <li>• Infection: sepsis, abdominal sepsis, wound infection, systemic infections.</li> <li>• Impaired renal and hepatic function</li> <li>• Bone marrow suppression</li> <li>• GIT bleeding</li> <li>• Pancreatitis</li> </ul>	<p>Consider the indication and seek any necessary advice. If feasible, withhold on the day of surgery and resume once renal function normal, usually within 3 days. Consider stopping if severe systemic infection occurs.</p>
<b>Ciclosporin</b>	<ul style="list-style-type: none"> <li>• Prophylaxis of transplant rejection</li> <li>• Inflammatory bowel disease</li> <li>• Rheumatoid Arthritis</li> <li>• Atopic dermatitis</li> <li>• Psoriasis</li> </ul>	<p>Risk of continuation:</p> <ul style="list-style-type: none"> <li>• Infection</li> <li>• Renal and hepatic toxicity</li> </ul> <p>Risk of stopping</p> <ul style="list-style-type: none"> <li>• Organ rejection</li> <li>• UC flare up</li> </ul>	<p>Continue – administer a dose 4 – 7 hours pre-op and continue during the peri-operative period. Monitor closely for renal and hepatic impairment. Avoid use of NSAIDS Consider drug interactions and formulation changes – consult pharmacy for advice.</p>
<b>Hydroxychloroquine</b>	Rheumatoid arthritis	<p>Risk of flare up of condition if stopped</p> <p>Risk of hypoglycaemia</p>	<p>Continue treatment</p> <p>Monitor for hypoglycaemia</p>
<b>Mercaptopurine</b>	<ul style="list-style-type: none"> <li>• Acute Leukaemias (ALL and AML)</li> <li>• Chronic leukaemias</li> <li>• Chrons and Ulcerative colitis</li> </ul>	<p>Risk of continuation:</p> <ul style="list-style-type: none"> <li>• Hepatotoxicity</li> <li>• Bone marrow suppression</li> <li>• Pancreatitis</li> <li>• Hyperuricaemia</li> </ul> <p>Risk of stopping</p> <ul style="list-style-type: none"> <li>• Crohns or UC flare up</li> </ul>	<p>Patients should be individually assessed and relevant advice sought. If to be held: Omit on the day of surgery and resume post-operatively once renal function is stable. Consider stopping if significant systemic infection occurs. Withdraw if jaundice occurs.</p>
<b>Methotrexate</b>	<ul style="list-style-type: none"> <li>• Rheumatoid Arthritis</li> <li>• Psoriasis</li> <li>• Haematological conditions and cancers</li> <li>• Severe Crohns</li> <li>• Prevention of rejection in bone marrow transplants</li> </ul>	<p>No evidence for increased infection rates when used as a single agent.</p>	<p>Weekly methotrexate should not usually be discontinued. If concerned, consult the doctor responsible for the patients care. Monitor renal and hepatic function.</p>

Drug	Indications	Risks associated with surgery	Advice
<b>Biological agents</b> - <b>Infliximab</b> - <b>Adalimumab</b> - <b>Tocilizumab</b> - <b>Etanercept</b> - <b>Golimumab</b> - <b>Abatacept</b> - <b>Secukinumab</b> - <b>Ustekinumab</b>	<ul style="list-style-type: none"> <li>• Rheumatoid Arthritis</li> <li>• Crohns disease</li> <li>• Ulcerative colitis</li> <li>• Psoriasis</li> <li>• Psoriatic arthritis</li> <li>• Ankylosing spondylitis</li> </ul>	These drugs impact on the immune system, so there may be an increased risk of infection. The available evidence is very mixed. The risk of stopping may be greater than the risk of continuing the medication, particularly in severe inflammatory conditions.	Advice should always be sought from the consultant responsible for the patients care. Some sources state that if stopped, this should be for 2 drug cycles prior to elective surgery.

## 8. CENTRALLY ACTING DRUGS

Centrally acting drugs include 4 main categories:

- Opioids
- Anti-epileptic medications
- Anti-parkinsons medications
- Antidepressant medications.

Each group will be considered separately.

### 8.1 Opioids

Drugs to be considered are those that are prescribed for chronic pain, and include Buprenorphine and Fentanyl patches and oral morphine and oxycodone.

Additionally a patient may be taking opioids bought 'off the street' for recreational use. These could additionally include heroin (diamorphine), and may be injectable, or they may be undergoing treatment for opioid addiction, usually with either methadone or oral buprenorphine.

If a patient is on regular opioid therapy for any indication, it is important that the anaesthetist is made aware prior to the procedure as this may have an impact on the choice and dose of analgesic used during and immediately post procedure.

#### Topical opioids (patches)

- In most cases, the patient should continue with these as usual
- The patient should be monitored for signs of toxicity post-operatively
- Symptoms of toxicity can include respiratory depression, over sedation, hypotension
- If it is felt necessary to remove the patches, it should be noted that the drug concentrations fall slowly and it takes 17 hours or more for serum concentrations to decrease to 50%.

### Modified release (mr or XL) preparations

- Patients on opioids for chronic pain relief should have missed doses minimised.
- General advice is that modified release preparations of morphine and oxycodone are not given in the immediate pre-operative period or in the first 24 hours post-operatively. This is due to the unpredictable effects on bowel motility. This can be a particular problem in bowel surgery and increases the risk of ileus.
- Patients may require higher than usual doses of analgesia post-operatively if they are on regular doses of strong opioids.
- Patients should be monitored closely for signs of toxicity.
- It may be necessary to use alternative routes of administration post operatively.

### Recommendation

- Advise patients to omit their morning dose of a modified release opioid.
- Pain control will then be managed post-operatively by the most appropriate team.

Please note, some enhanced recovery programmes include modified release opioids (Oxycodone MR). This has been shown to be of benefit in these programmes at the prescribed doses.

### Patients using opioids recreationally

- Due to the fact that it is difficult to determine the actual dose of opioid being taken by patients using them recreationally, they should be treated as any other surgical patient
- Post-operatively, they are likely to have degree of tolerance so higher doses may be required
- Opioid addiction is not a reason to withhold opioids in post-operative patients
- It is important to closely monitor the patients to ensure their pain is adequately controlled.

### Patients on Methadone Programmes

- The usual dose should be taken on the morning of the surgery
- If the patient is on a methadone programme this should be clearly documented pre-operatively
- The following information should if possible be recorded: details of the clinic they get their prescriptions from, details of the pharmacy supplying the medication
- The dose taken should be confirmed on admission or post-operatively with the clinic or chemist
- Post-operatively, methadone should be prescribed at the patients usual confirmed dose and pain relief provided as with any other post-operative patient.

## 8.2 Anti-epileptic medications

Anti-epileptics should not be omitted prior to surgery due to the risk of fitting for the patients.

Post-operatively, where possible, the patient should be put back onto their usual medications. If this is not possible then advice should be sought from pharmacy urgently (including on-call) for alternatives.

## 8.3 Anti-parkinsons medication

Anti-parkinsons medications include:

- Levodopa – usually in combination preparations co-beneldopa and co-careldopa
- Entacapone
- Ropinarole
- Pramipexole
- Amantidine
- Rotigotine
- Apomorphine
- Rasagiline

Parkinsons patients are high risk surgical patients. There is an increased risk of aspiration pneumonia and post-operative respiratory failure, which is exacerbated further if doses of medication are delayed or missed.

Additionally, there is a risk of precipitation of neuroleptic malignant syndrome if these drugs are stopped suddenly. This is more likely in Levodopa containing preparations which have a short half-life.

Continuation of Parkinsons medications in the peri-operative period carries its own risks, with an increased likelihood of arrhythmias and blood pressure fluctuations. In the majority of cases, these risks of exacerbation of Parkinsons symptoms is greater than the risk of continuing medication.

### Peri-operative management:

In Parkinsons patients surgery should be planned to allow predictability in operation time in order to minimise any NBM period. Oral drug therapy should be continued as close to the procedure as possible, ideally allowing any morning dose to be administered with a small amount of water. Patients receiving topical treatment (patches) should keep these in-situ throughout the peri-operative period.

### Post-operative management

Parkinsons medication should be restarted as soon as possible following the procedure to minimise missed doses. Failure to reinstate therapy can lead to issues as above, and additionally can delay recovery due to the inability of the patient to undertake required therapy (physio or OT).

If a patient is unable to take oral medication, due to either swallowing difficulties or the nature of the surgery, please refer to the attached document: <http://bhftintranet.burtonft.nhs.uk/Departments/pharmacy/prescribing%20tips%20page/Parkinsons%20disease%20Guidelines%20for%20the%20inpatient%20management%20of%20medicines.pdf>

Alternatively, contact pharmacy to discuss options.

#### **8.4 Antidepressant medication**

Drug groups covered in this section include:

- Benzodiazepines (e.g. Diazepam, Lorazepam etc.)
- SSRI's (e.g. citalopram, fluoxetine)
- Monoamine oxidase inhibitors (MAOI) (e.g. Phenelzine)

Antidepressant drugs are listed in the BNF in categories, so if you are unsure which group a drug belongs to please check.

##### Benzodiazepines

Benzodiazepines are used as anxiolytics, hypnotics, and in some cases for the treatment of epilepsy and status epilepticus. Additionally, they are often used as premedication or induction agents in theatres.

##### Advice

- The anaesthetist should be made aware that the patient is a regular user of benzodiazepine medication
- It is important that the indication is determined, if a patient is taking a benzodiazepine for epilepsy treatment this should be treated as in Section 8.2
- For patients on long term benzodiazepines, withdrawal symptoms may start to occur within 24 hours of stopping medication, so if there is prolonged period of nil-by-mouth, use of an alternative benzodiazepine that can be administered parenterally can be considered
- Benzodiazepines usually taken for night sedation can be safely administered on the night before surgery.

##### SSRI's

SSRI's are indicated for the treatment of depressive illness.

##### Advice

- SSRI's should not be stopped abruptly due to the risk of withdrawal effects associated with these drugs. Treatment should therefore be continued in the peri-operative period
- There is evidence of an increased bleeding risk with these drugs, so NSAIDs should be used with caution. If necessary, prescription of a PPI should also be considered
- Caution with administration of serotonergic drugs (e.g. fentanyl, oxycodone, pethidine, tramadol) as this increases the risk of serotonin syndrome

- Additionally, co-administration with tramadol may lower the seizure threshold, particularly in patients who have any underlying condition predisposing them to seizures.

### MAOI's

These drugs are rarely used, but are indicated for depressive illness. They are long acting drugs with effects lasting for up to 2 weeks after cessation of therapy.

The main risks in surgical patients on these drugs are:

- Serotonin syndrome
- Hypertensive crisis

### Advice

- For elective surgery, the patient should be discussed with the anaesthetist at the earliest opportunity.
- For emergency surgery, the anaesthetist must be informed ideally prior to anaesthesia being administered.
- MAOI safe anaesthesia should be used – all inhalation anaesthetics are safe.
- Manufacturers of Phenelzine and Tranylcypromine recommend that the drug should be discontinued 2 weeks prior to elective surgery. This should always be done in consultation with the patients psychiatrist.
- The opioid of choice is Morphine which should be used cautiously at low doses. Tramadol should be avoided as it lowers the seizure threshold.
- Avoid Suxemethonium, Phenelzine, Pethidine, Cocaine and Ketamine.

## **9. HORMONAL THERAPY**

This drug covered in this section include:

1. Tamoxifen and Raloxifene
2. Hormone Replacement therapy
3. Combined oral contraception
4. Progesterone only contraception.

### **9.1 Tamoxifen and Raloxifene**

#### Risks

- There is some evidence that these drugs can increase the risk of VTE in patients undergoing surgery. Combined with an increased risk of VTE in patients with breast cancer.

#### Advice

- Individual cases should be discussed with the breast / oncology consultant responsible for the patients care. Dependent on the type and duration of surgery and other patient risk factors, the drug may be stopped for up to 6 weeks around the period of surgery.

## **9.2 Hormone Replacement Therapy (HRT)**

### Risks

- Oral HRT is associated with a 1.3 – 3 fold increased risk of developing VTE in non-surgical patients. This risk is greater with combined HRT (patients who still have a womb). The level of risk with topical HRT (patches) has not been established, but is thought to be lower.

### Advice

- In light of VTE risk many sources advise stopping HRT 4 – 6 weeks before major surgery, particularly if there is a likelihood of prolonged immobilisation. There is however little evidence comparing continuation of HRT with withdrawal of HRT in the peri-operative period and there is no compelling evidence that HRT should be discontinued in the peri-operative period
- The risks and benefits should be discussed with the patient and a decision made dependant on their feelings related to the impact on quality of life and the risk of VTE
- If HRT is discontinued, it should not be restarted until the patient is fully mobile.

## **9.3 Combined oral contraception (COC)**

### Risks

- There is an increased risk of VTE and ischaemic stroke in patients using COC's. This risk increases with age and other risk factors such as obesity and thrombophilia status.

### Advice

- The risks are as those for HRT. Please follow the advice in this section. If a patient feels it is necessary to withhold their COC, they can be restarted at the first menses occurring at least 2 weeks after full mobilisation
- Alternatively a POP can be used. The patient would need to see their GP if this is their preferred option.

## **9.4 Progestogen only contraception (POP)**

### Risks

- There is no evidence of an increased risk of VTE with POP's.

### Advice

- POP's are recommended as an alternative to COC's in surgical patients. Therefore it is safe to continue them in the peri-operative period.

## 10. REFERENCES

The Handbook of Peri-Operative Medicines – UK Clinical Pharmacy Association and Royal Pharmaceutical Society. August 2016

Perioperative management of anticoagulation and antiplatelet therapy.  
British Society for Haematology.(BCSH) 2016

Buckinghamshire Healthcare NHS Trust, Chiltern CCG, Aylesbury Vale CCG.  
Guidelines on Peri-operative Bridging of Warfarin Therapy in Adult Patients  
Undergoing Elective Surgery or Invasive procedures. October 2016



## **Calculation of CHA<sub>2</sub>DS<sub>2</sub>VASc score in patients with Atrial Fibrillation**

To determine the risk of stroke in a patient with atrial fibrillation, the CHA<sub>2</sub>DS<sub>2</sub>VASc score should be calculated. The score should be calculated using the following table for all patients with Atrial Fibrillation. Points should be added and documented in the notes when recording any decision made around anticoagulation.

You would expect all patients with Atrial fibrillation and a CHA<sub>2</sub>DS<sub>2</sub>VASc score of 1 or more (men) or 2 or more (women) to be on anticoagulation. The maximum score is 9, and the risk of stroke increases from 1.3% with a score of 0 to 15.3% with a score of 9.

<b>Condition</b>	<b>Points</b>	<b>Score</b>
<b>C</b>	Congestive heart failure (or Left ventricular systolic dysfunction)	<b>1</b>
<b>H</b>	<a href="#">Hypertension</a> : blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	<b>1</b>
<b>A<sub>2</sub></b>	Age ≥75 years	<b>2</b>
<b>D</b>	Diabetes Mellitus	<b>1</b>
<b>S<sub>2</sub></b>	Prior <a href="#">Stroke</a> or <a href="#">TIA</a> or <a href="#">thromboembolism</a>	<b>2</b>
<b>V</b>	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	<b>1</b>
<b>A</b>	Age 65–74 years	<b>1</b>
<b>Sc</b>	Sex category (i.e. female sex)	<b>1</b>

## **Calculation of estimated Creatinine Clearance**

Creatinine clearance can be estimated using the following calculation:

$$\text{Approx. CrCl (ml/min)} = F \times \frac{(140 - \text{age}) \times \text{wt(kg)}}{\text{Creatinine}}$$

Where F = 1.23 in males and 1.04

Please note: When estimating a creatinine clearance for an obese patient an estimate of the non-obese or ideal body weight (IBW) should be used.

Ideal body weight for males in kg = 50 + (2.3) (height in inches > 60)

Ideal body weight in females in kg = 45 + (2.3) (height in inches > 60)

Adjusted body weight (ABW) should be used in morbidly obese

$$\text{ABW} = \text{IBW} + 0.4 (\text{TBW} - \text{IBW})$$

$$\text{TBW} = \text{Total Body Weight}$$

**Prophylactic doses of Enoxaparin**

<b>Bodyweight</b>	<b>Enoxaparin dose</b>
< 50 kg	20 mg OD*
51 – 100 kg	40 mg OD
101 – 150 kg	40 mg BD*
>150 kg	60 mg BD*

\* Unlicensed doses

For patients with renal impairment the following guidance should be followed:

- *eGFR > 30 ml/min – no dose adjustment required.*
- *eGFR – 15 to 30 ml/min – halve dose of Enoxaparin for prophylaxis of DVT.*
- *eGFR <15 ml/min – Contact the consultant haematologist for advice*

**Treatment doses of Enoxaparin in High thromboembolic risk patients**  
**For Patients with a metallic valve replacement**

Note: these patients will always be on Warfarin

Twice daily Enoxaparin is required in these patients at a dose of 1mg/kg BD. The dose should be rounded to the nearest full syringe to aid administration and patient compliance. See the table below:

<b>Patient Weight</b>	<b>Enoxaparin Dose</b>
40 – 50 kg	40 mg BD
51 – 70 kg	60 mg BD
71 – 90 kg	80 mg BD
91 – 110 kg	100 mg BD
111 – 135 kg	120 mg BD
136 – 160 kg	150 mg BD
>150 kg	Seek haematologist advice

**Treatment doses of Enoxaparin in High thromboembolic risk patients**  
**For other high risk patients**

Once daily Enoxaparin is required the usual dose given to this group of patients is between 1mg/kg OD and 1.5mg/kg OD. Doses are rounded to the nearest full syringe as above. See table below:

<b>Patient Weight</b>	<b>Enoxaparin Dose</b>
<46kg	40 mg OD
46 – 56kg	60 mg OD
57 – 68 kg	80 mg OD
69 – 82kg	100 mg OD
83 – 110 kg	120 mg OD
111 – 130 kg	150mg OD
>131kg	Seek haematologist advice

