Peri-operative Drug Management Guidelines

Policy Title:	Peri-operative Drug Management Guidelines
Executive Summary:	This policy provides guidance on which drugs should be given peri-operatively and which drugs should be temporarily withheld.
Supersedes:	Version 11
Description of Amendment(s):	Version 12 Amendments: • Aspirin – addition of wording for breast surgeons • Clopidogrel page 9-10, removal of word breast surgeon • Prasugrel - page 16, removal of word breast surgeon • Ticagrelor page 17, removal of word breast surgeon
This policy will impact on: Drug management for all patients admitted for elective surgery. Recommendations of policy impact on surgical patients. Healthcare professionals managing surgical patients (doctors/ nurses/pharmacist) should be familiar with policy recommendations	
Financial Implications: Limited financial impact. Resources required in the form of policy writers will have to review their policies to ensure that they meet the guidance contained in this document.	

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Introduction

Evidence collected by the National Confidential Enquiry into Peri-operative Deaths (NCEPOD) suggests that peri-operative drug management is not currently optimal and omission of important medication may contribute to post-operative mortality. Omission of regular drug therapy may cause exacerbation of the underlying pathology or withdrawal symptoms which may compromise patient outcome. NCEPOD suggests that patients do not receive essential medication pre-op owing to staff misinterpreting the term “nil by mouth” (NBM).[1]

What does NBM mean?

- Clear fluids (water/squash) – none in 2 hours prior to surgery (except for 30mL to administer medication.
- Food (includes milk) – none in the 6 hours prior to surgery (Except for enhanced recovery patients who take nutritional supplement drinks which may be given up to TWO hours pre op)
- Medicines –regular medication should be administered up to 1 hour prior to surgery with 30mls of water unless they need to be withheld.

(If in any doubt please ask the Anaesthetist for that list or a pharmacist)

Pre-admission clinic/admitting doctor’s responsibilities:

Peri-operative pharmaceutical management decisions should not be made on the morning of surgery. It is important that planning begins earlier at the pre-op assessment stage so that certain drugs which require discontinuation for longer periods of time pre-op can be managed effectively. Owing to potential interactions with anaesthetic agents and regular drugs, a thorough drug history must be completed so that the anaesthetist is aware of all drugs, including herbal medicines and supplements, which the patient is taking. If steroid medications have been discontinued within the previous three months this must also be documented in the medical notes/back of drug chart for the anaesthetist’s attention.

It is mandatory that an accurate and complete drug chart is written pre-operatively for the anaesthetist’s attention. Please refer to this guideline to decide on a pharmaceutical management plan for the patient. In certain situations the drug may be administered by a different route or alternative product. This guideline does not give advice on how to manage medication. If a patient is unable to take it by normal route post operatively then please ask advice from a pharmacist.

Summary Guidelines For the management of Drug Therapy in the Peri-operative Period

This table below is a summary of the guidelines for the management of drug therapy in the peri-operative period. For further guidance please discuss with a pharmacist or anaesthetist.

Drug	Recommendation	Comments	Alternative Route if oral unavailable
Acomprosate	**Continue**		
Allopurinol	**Continue**		
Alpha Blockers e.g. doxazosin, tamsulosin	**Continue** **In cataract surgery continue but alert the ophthalmologist (Risk of Intraoperative floppy iris syndrome (IFIS) in these patients)**		
Antianginals (Nitrates, nicorandil, calcium channel antagonists)	**Continue**	May precipitate chest pain if withheld	Convert nitrates to patch and use buccal for chest pain.
Antiarrythmics (Amiodarone, digoxin, flecainide)	**Continue**	Possibility of recurrence of arrhythmias if stopped. Check Digoxin levels	IV form available require careful monitoring
Anticoagulants (oral) ***(Warfarin, phenindione, acenocoumarol)***	**SEE FLOWCHART FOR PERI-OPERATIVE ANTICOAGULATION IN APPENDIX 1**		
Anticonvulsants (Phenytoin, sodium valproate, carbamazepine)	**Continue**	Possibility of precipitating convulsions if stopped. Ensure prn diazepam Rx.	Intravenous and rectal forms available- not all bioequivalent.
Antidepressants (Tricyclics, SSRIs) NOT MAOIs	**Continue**	Withdrawal symptoms can occur if stopped abruptly.	Monitor for withdrawal symptoms- no alternative forms available.
Antipsychotics (Haloperidol, Chlorpromazine)	**Continue**	Withdrawal symptoms and severe agitation can occur if stopped abruptly	IV forms available. May also need prn doses prescribing

Drug	Recommendation	Comments	Alternative Route if oral unavailable
Aspirin	***Minor Surgery:Continue*** ***Major surgery :Continue*** ***(except for Breast /ENT /Shoulder/ Urology Surgery and ophthalmology procedures see notes below)*** ***Aspirin for primary prevention -Stop 7 days pre-op*** ***Aspirin for secondary prevention-Continue*** *(Please email Surgeon to continue aspirin as per cardiology advice).* ***Aspirin for coronary stents: Continue*** ***Patients on aspirin for Stroke/TIA-Continue*** ***Patients on aspirin for AF: Stop aspirin pre-op for 7 days as per cardiology advice.*** ***Patients on aspirin for Peripheral Vascular Disease: Continue*** ***Ophthalmology procedure/surgery e.g. cataracts: Continue(For more complex opthalmic procedures liase with opthalmologists)*** ***Shoulder Surgery: Continue*** **Urology Surgery:** ***Continue (If patient on doses>75mg OD liaise with urology)*** **ENT Surgery** - surgeons will document whether they will stop or continue aspirin	**Restart when risk of bleeding no longer significant (usually ~3-4 days post-op)**	

Drug	Recommendation	Comments	Alternative Route if oral unavailable
Aspirin (continued)	**Breast Surgery** – **Aspirin should not be discontinued for breast surgical procedures (in patients taking it for primary or secondary prevention)** – unless the breast surgeon gives a valid written reason for discontinuing		
Antiretrovirals	**Continue – Never change, omit or stop without explicit instructions from a specialist consultant Physician in HIV medicine.**	Some antiretrovirals may affect the metabolism of some anticoagulants so always check interactions on: www.hiv-druginteractions.org	Contact Refer to specialist consultant/ centre or Anne Neary Lead Pharmacist Antimicrobials, Infectious Diseases and Sexual Health Tel : 07834368956 Anne.neary@liverpoolft.nhs.uk
ACE & Angiotensin 2 receptor antagonists i.e. ramipril, perindopril, candesartan, losartan Also includes Entresto	**Omit morning dose on day of surgery** (Continue evening doses)	Restart next day if not NBM	
Beta blockers	**Continue**		Injections are available of some drugs only- may need to be changed to an alternative drug if oral route not possible
Benzodiazepines (Diazepam, lorazepam)	**Continue**	Withdrawal symptoms can occur if stopped abruptly	Rectal and IV forms available.
Bisphosphonates i.e. alendronic acid, risedronate	**Omit on morning of operation**	Only recommence when patient is able to sit upright and is drinking free fluids.	

Drug	Recommendation	Comments	Alternative Route if oral unavailable
Bronchodilators (Salbutamol, ipratropium, theophylline)	**Continue**	May precipitate bronchospasm if withheld.	Use nebules. Can convert oral to IV aminophylline if necessary.
Calcium channel blockers *e.g. amlodipine, diltiazem*	**Continue**	May precipitate chest pain if withheld.	
Corticosteroids *Includes oral, inhaled, topical*	See Appendix 5 - **Criteria for patients who need pre- and post-operative steroid cover** See Appendix 6 – **Surgical Guideline for Management of patients on Corticosteroids**	Ensure guidance is followed Increased risk of Addisonian crisis if stopped	
Clopidogrel	**N.B Please see Appendix 2 (p20) - Policy for patients having elective surgery who are taking anti-platelet agents *and* who have a coronary stent.** **Shoulder Surgery -** ***Continue*** ***Ophthalmology procedure/surgery e.g. cataracts: Continue (For more complex ophthalmic procedures liaise with ophthalmologists)*** **ENT Surgery**- Surgeons will document in notes and booking form whether they will stop or continue clopidogrel ***For patients on Clopidogrel for Stroke /TIA*– that occurred >9 months ago- Stop 7 days pre-op. Bridge with Aspirin 75mg daily if tolerated**-(If CVA/TIA	**Restart when risk of bleeding no longer significant (usually ~3-4 days post-op)** **Restart when risk of bleeding no longer significant (usually ~48hrs post-op)**	

Clopidogrel (continued)	<9/12 ago –Discuss with anaesthetist) **Cardiac indication -** Discuss with the cardiology team ***Patients on clopidogrel for PVD (Peripheral Vascular Disease)-*** **Stop 7 days pre-op. Bridge with Aspirin 75mg daily if tolerated**	**Please note patients on clopidogrel, prasugrel and ticagrelor may have a new stent in place or have had a coronary event in which surgery may not be suitable hence discussions needed with cardiology team**)	
Clozapine	**Liaise with Psychiatric team**		
Combined oral contraceptives ***(e.g. Loestrin, Logynon, Microgynon, Ovran, Marvelon, Minulet, Brevinor, Cilest)***	**Minor Surgery or those which will not immobilise the patient post-op -Continue** For **major elective** surgery which has had a high thrombotic risk e.g. major joint surgery/ previous VTE or any surgical procedure which will immobilise patients - **to stop 4 weeks pre-op** **Ensure patients are prescribed LMWH prophylaxis and TEDS**	For patients who have withheld pre-op to restart on discharge. Ensure patient takes extra contraceptive precautions as per BNF recommendations	
COX II inhibitors **(celecoxib, etoricoxib**	**Continue**		

Drug	Recommendation	Comments	Alternative Route if oral unavailable
Cytokine modulators and Anti-TNF dugs **Etanercept** **Adalimumab & others** **See BNF** **Cytokine modulators and Anti-TNF dugs continued**	**Etanercept - Stop 2 weeks pre-op** **Adalimumab - Stop 2 weeks pre-op** **Certolizumab and golimumab- Omit one dose before surgery.** **Other cytokine modulators/ Anti TNF drugs - Discuss with Rheumatologist**	**For etanerecept and adalimumab** ↓ **Refer to Rheumatologist** **For Certolizumab and golimumab** ↓ **Restart 2 weeks post op if there is no evidence of infection & the patient is not on antibiotics. If signs of infection or patient on antibiotics >2 weeks post-op - consult rheumatologist**	
Desmopressin	**Continue**		
Drugs for dementia ***Donepezil***	**Continue- INFORM ANAESTHETIST** Donepezil is known to have interactions with muscle relaxants but there is a risk of cognitive decline if stopping it for three weeks+.	**If stopped re-start as soon as possible post-op**	(Remifentanil indicated in theatre for these patients
Drugs for dementia Rivastigmine/ Galantamine	**Stop 24 hrs pre-op**		
Drugs for erectile dysfunction i.e. sildenafil, tadalafil	**Avoid 24 hours before surgery** EXCEPT for pulmonary hypertension **CONTINUE** ensure anaesthetist aware of use	**Vasodilator properties leading to mild and transient hypotension**	

Drug	Recommendation	Comments	Alternative Route if oral unavailable
Oral diabetic medication/non-insulin injections	**See Appendix 3 - Minor/ Major Surgery**	Restart oral hypoglycaemics once patient eating and drinking.	
Dipyridamole	**Stop 24 hours pre-op**	Restart when risk of bleeding no longer significant (usually ~3-4 days post-op)	
Direct Oral Anticoagulants (DOAC) **Rivaroxaban, Apixaban, Dabigatran, Edoxaban**	**See ECT Treatment and prevention of VTE guidelines Appendix 1**	Restart when risk of bleeding no longer significant (usually ~3-4 days post-op)	
Diuretic **(Thiazide & Loop) i.e Furosemide, bendroflumethazide**	**Continue**		**Some IV injections are available**
All DMARDs and immunosuppressants e.g. azathioprine methotrexate, cyclophosphamide leflunomide (See BNF)	**The same advice for methotrexate also applies to all other immunosuppresants** For **RA and dermatology** patients on methotrexate • Check renal function within 6 weeks of any planned operation • **If the eGFR is > 30 ml/min then methotrexate should be omitted the week before and the week after surgery** provided the patient is making satisfactory progress and is not on antibiotics post operatively • Renal function should be checked again post-operatively and if it has not deteriorated then the same dose of methotrexate can be re-started if the patient is making satisfactory progress. • If the patient is more likely to be on antibiotics post operatively for >1	7 days post op when eating and drinking (providing the patient is making satisfactory progress) and no concerns with wound infection or deranged blood test results **FBC/ U&E's/ LFT's & eGFR should be checked post op major surgery** Patients should be informed in writing at their pre-op assessment when they should omit their methotrexate. They should also be informed that any stop of treatment is only short-term and that they should	

	week – consult Rheumatologist. • **If the eGFR is ≤ 30ml/ min then all medications should be discussed with the rheumatologist prior to surgery.** • Patient should not stop their methotrexate for more than 2 weeks without good reason. The Rheumatologist should be consulted in this situation	expect to be taking the same dose of methotrexate when they go home as when they came into hospital. They should continue to take their usual dose of folic acid throughout.	
Drugs of abuse	**ENSURE ANAESTHETIST IS AWARE IF ILLICIT DRUG USE IS STRONGLY SUSPECTED**		
Finasteride	**Continue**		
Immuno-modulators e.g sulfasalazine and hydroxychloroquine	**Omit dose on morning of surgery**		
Herbal medicines (e.g. Garlic, Ginseng, Gingko, St Johns Wort)	**Stop 2/52 pre-op. See appendix 8**		
H2 Blockers (Ranitidine, nizatidine, famotidine)	**Continue**		
HRT ***(including tablets, implants, and Raloxifene)*** **Transdermal include gels, patches**	**For minor surgery – Continue** Ensure patients are prescribed LMWH prophylaxis and TEDS **For major elective surgery** which has had a high thrombotic risk e.g. major joint surgery/previous VTE or any surgical procedure which will immobilise patients - **to stop 4 weeks pre-op** **Except - continue if on transdermal route for oestrogen**	**Restart when patient fully mobile** **Ensure patients are prescribed LMWH prophylaxis and TEDS**	
Ibrutinib	**Stop 7 days pre and post op**		

Drug	Recommendation	Comments	Alternative Route
Immunomodulators e.g. sulfasalazine and hydroxychloroquine	**Omit dose on day of surgery morning**		
Insulin	**See Appendix 4 –Minor /Major surgery**		
Ivabradine	**Continue**	Monitor heart rate, avoid use of ondansetron	
Lithium	Omit morning dose on day of surgery **Check U&Es pre-op** Continue with close monitoring of fluid balance and U+E's as Lithium toxicity may develop in patients with deranged electrolytes.	**Restart as soon as possible post-op** **Will require close monitoring of fluid balance and U+E's post-op to avoid lithium toxicity**	
Mercaptopurine	**Continue**	**Monitor the patient for infection – consider withholding mercaptopurine if patient develops a significant systemic infection - contact patient's specialist for advice.** **Monitor U&E's closely - Withhold if renal function deteriorates in the post-op period and contact patient's specialist for advice.**	
Irreversible MAOI **eg Phenelzine, isocarboxazid, Tranylcypromine**	**INFORM ANAESTHETIST** May decide to use MAOI "safe" anaesthesia or to stop 2/52 pre-op with careful discussion with psychiatrist	**Restart 48 hours post-op** **If continuing need to avoid opioids during post-op period**	

Drug	Recommendation	Comments	Alternative Route
Reversible MAOI **(Moclobemide)**	**INFORM ANAESTHETIST** May decide to use MAOI "safe" anaesthesia or to stop 24 hours pre-op	**Restart 24 hours post-op** **If continuing need to avoid opioids during post-op period**	
Selective MAOB inhibitors e.g. Rasagiline	**INFORM ANAESTHETIST** Stop 24 hours pre-op	**Restart 24 hours post-op** **If continuing need to avoid opioids during post-op period**	
Mycophenolate mofetil	**Continue**	**Inform patient's relevant specialist of admission**	
NSAID's	***Short-acting agents e.g. Ibuprofen, Diclofenac:*** **stop 1 day pre-op** ***Long-acting agents e.g. Piroxicam, Naproxen:*** **stop 4 days pre-op** **For major orthopaedic surgery stop 4-7 days pre-op according to Consultant preference**	**Restart when risk of bleeding no longer significant (usually ~3-4 days post-op)**	
Opioids	***• In general to continue but always liaise with pain team (bleep 3402)*** ***• Fentanyl patch - continue, keep patch applied to patient*** ***• Buprenorphine patch - continue, keep patch applied to patient*** ***• Methadone – continue*** **(Methadone dose to be confirmed by CDT before commencement. Out of hours refer to Management of Drug users admitted to hospital policy. Please refer to intranet under Guidelines/Medications/Management of Drug Misusers admitted to hospital ECT3776)**	**Liaise with pain team (Bleep 3402)** **Inform pain team of these patients & Anaesthetist** **Inform rehab centre**	
Orlistat	***Omit whilst NBM. Restart once patient eating***		

Drug	Recommendation	Comments	Alternative Route
Parkinsons medication (Except Rasagiline-see pg 15 MAOB inhibitors) (Madopar, Sinemet)	**Continue as usual** (Except Rasagiline-see pg 15 - MAOB inhibitors)	Movement disturbances will return on withdrawal of treatment.	Apomorphine injection available but for specialist use only- very emetic.
Potassium-sparing Diuretics *(Spironolactone, Amiloride)*	**Omit morning dose on day of surgery**	**Restart morning dose next day**	
Progestogen-only pills and contraceptive depot injections ***(Femulen, Micronor, Microval, Neogest, Norgeston, Noriday, Depo Provera, Noristerat)***	**Continue**		
Proton Pump Inhibitors (lansoprazole, omeprazole, pantoprazole)	**Continue**	Essential prior to anaesthesia	Pantoprazole and omeprazole available as injection
Prasugrel	**Discuss with cardiology team** ***For patients who are undergoing ophthalmology procedure e.g cataracts Continue(For more complex opthalmic procedures liase with opthalmologists)*** **ENT Surgery**- surgeons will document in notes and booking form whether they will stop or continue Prasugrel	(Please note patients on clopidogrel, prasugrel and ticagrelor may have a new stent in place or have had a coronary event in which surgery may not be suitable hence discussions needed with cardiology team)	
Pyridostigmine	**Continue for Myasthenia Gravis** Other all other indications discuss with an anaesthetist. **INFORM ANAESTHETIST**	Anticholinesterases prolong the action of depolarising neuromuscular blocker agents. Suxamethonium should be avoided.	

Drug	Recommendation	Comments	Alternative Route
Ranolazine	**Continue**		
Statins e.g atorvastatin, simvastatin, pravastatin	**Continue**		
Tamoxifen	**Breast cancer**: Tamoxifen stop ONE month before surgery. **Anovulatory infertility**: Stop 6/52 pre-op as advised	**Restart when patient fully mobile**	
Other aromatase inhibitors (except Tamoxifen) e.g. Letrozole, Exemestane (See BNF)	**For minor and major surgery – Continue** Ensure patients are prescribed LMWH prophylaxis and TEDS		
Ticagrelor	**Patients who are having surgery<1 year post cardiac event -**discuss with cardiology team **If surgery> 1 year post infarction and patient does not have a coronary stent then** stop 5 days pre –op and continue with aspirin if on dual antiplatelet therapy ***Ophthalmology procedure/Surgery e.g cataracts Continue (For more complex opthalmic procedures liase with opthalmologists)*** **ENT Surgery** - surgeons will document in notes and booking form whether they will stop or continue ticagrelor	(Please note patients on clopidogrel, prasugrel and ticagrelor may have a new stent in place or have had a coronary event in which surgery may not be suitable hence discussions needed with cardiology team)	
Thyroid medication (Levothyroxine, carbimazole, Propylthiouracil)	**Continue**	Both have 3-4/7 half-life. After this time need replacing.	Levothyroxine→ IV liothyronine (not bioequivalent). No commercially available PR or IV carbimazole.

Drug	Recommendation	Comments	Alternative Route
Vaccines ***Covid -19*** ***Influenza***	**Essential urgent surgery** should take place, irrespective of vaccination status. **Non-urgent elective surgery**: ideally separate the date of surgery from vaccination by at least 3-4 days.		

Appendix 1

Please see VTE guidelines .Click here (Guidelines for the prevention and treatment of venous thromboembolism (VTE) in medical and surgical patients)

See Appendix 2 of VTE guidelines for:

- **Peri-operative anticoagulation guidelines for patients admitted on anticoagulation undergoing elective surgery /CHADS 2 scores.**
- **Peri-operative management of patients on anticoagulant therapy who require urgent surgery.**
- **Flow chart for managing cancelled elective patients on anticoagulant treatment**

See Appendix 5 of VTE guidelines for:

- **Guidance for stopping and starting New Oral Anticoagulants (NOAC's) in the peri-operative period**

Patients on Medicines that interact with Apixiban

The East Cheshire NHS Trust VTE Policy recommends that patients undergoing a hip or knee replacement are prescribed apixiban 2.5mg twice daily as the thromboprophylactic agent of choice.

However, in patients who are concurrently on drugs that interact with apixiban (as listed in the SPC); the patient will be prescribed appropriate dose of prophylactic LMWH post-operatively.

The SPC for apixiban advises the following:

The use of Eliquis is not recommended in patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp, such as azole-antimycotics (e.g., ketoconazole, itraconazole, voriconazole and posaconazole) and HIV protease inhibitors (e.g., ritonavir)

Co-administration of apixaban with rifampicin, a strong inducer of both CYP3A4 and P-gp, led to an approximate 54% and 42% decrease in mean apixaban AUC and $_{Cmax}$, respectively. The concomitant use of apixaban with other strong CYP3A4 and P-gp inducers (e.g., phenytoin, carbamazepine, phenobarbital or St. John's Wort) may also lead to reduced apixaban plasma concentrations.

Appendix 2

East Cheshire NHS Trust Surgical Business Unit
Policy for patients having elective surgery
who are taking anti-platelet agents *and* who have a coronary stent.

Summary:

- Clopidogrel / Ticagrelor or Prasugrel increases bleeding and depending on the surgery can be be stopped 5- 7days(as above guidance) before any elective surgery UNLESS THE PATIENT HAS AN INTRACORONARY STENT, when doing so can greatly increase the chance of stent thrombosis with a high mortality. At the moment we are only seeing a small number of patients presenting with a stent and taking clopidogrel.
- Clopidogrel /Ticagrelor or Prasugrel *should be continued perioperatively* in these patients unless the surgeon or anaesthetist feels that it would be a significant risk to do so. Such cases should be referred to Dr Egdell, Consultant Cardiologist.
- The risk of stopping clopidogrel / Ticagrelor or prasugrel in these circumstances is very variable, dependant on many risk factors and opinion is evolving. Appropriate courses of action, as well as continuing or stopping the drug, may include deferring or cancelling surgery or even performing it in another facility.

Clopidogrel:
Clopidogrel is a potent irreversible antiplatelet agent. Restoration of platelet function relies on the patient making new platelets, which takes a week. Bleeding can be treated by platelet transfusion because the plasma half-life (as opposed to the effect) of clopidogrel is short. Since its introduction, it has become clear that clopidogrel causes significant bleeding and it is usual practise to stop it one week before elective surgery. Clopidogrel has many indications. For nearly all of these it is clear that it should be stopped during the peri-operative period even for minor surgery. The one situation where this is not the case is if the patient has a coronary stent.

Clopidogrel is increasingly prescribed with aspirin following the 90% of percutaneous coronary interventions which now involve stents. PCI causes trauma to the vessel wall, activating platelets and causing coronary thrombosis if antiplatelet drugs are not used. There is increasing evidence that stopping clopidogrel *even for a short time* is a bad idea, particularly in the context of the peri-operative hypercoagulable state. Perioperative LMWH alone doesn't solve the problem.

This is not a minor issue. Non-cardiac surgery following stenting has been associated with a cardiac complication rate of up to 45% and a mortality of 5-20% in two recent major studies. The treatment for suspected stent thrombosis is urgent PCI, which is a difficult, risky procedure with a higher mortality than major bleeding.

Aspirin:
Aspirin is a lifelong therapy which should never be stopped after a coronary or cerebrovascular event. It may be stopped seven days prior to surgery if it is for primary prevention only. Neuraxial blocks are safe with up to 300mg per day of aspirin.[43]

Weighing up the risks:
The decision to stop antiplatelet therapy, particularly clopidogrel, depends on the balance of what the surgeon feels the risks and consequences of bleeding are if you don't, and what the cardiologists

think the risk of stent thrombosis is if you do. Anaesthetists must play a role in balancing these concerns.

Risks of stopping Clopidogrel, Ticagrelor or Prasugrel and causing stent thrombosis:

- Cessation of antiplatelet therapy is the major independent predictor of late stent thrombosis. This in turn has a 50% incidence of acute MI and 20% mortality.
- Although operating on patients taking clopidogrel or prasugrel increases bleeding considerably, it doesn't seem to increase morbidity, mortality, or surgical outcome. There is now good evidence that stopping it does.
- The risk is greater:
  - the more recently the stent was implanted
  - with drug eluting stents as opposed to bare metal stents
  - if the patient has other risk factors for stent thrombosis which are:
    - renal failure
    - diabetes mellitus
    - low ejection fraction
    - PCI involving bifurcation lesions or multiple drug eluting stents

PCI – PERCUTANEOUS CORONARY INTERVENTION

Risks of continuing clopidogrel, Ticagrelor or prasugrel and causing excessive bleeding:

- In non-cardiac surgery, patients on aspirin and clopidogrel or prasugrel and Ticagrelor have 25-40% increased risk of bleeding. Some studies however, have failed to show any difference.
- Clopidogrel / ticagrelor or prasugrel is an absolute contraindication to regional or neuraxial block. Neuraxial blocks are used extensively at ECNHS Trust for lower limb joint replacements and laparotomies. They provide superior pain relief and confer a morbidity / mortality advantage on high risk surgical patients. Not doing them may increase risk to the patient.
- Consideration should be given to stopping clopidogrel or prasugrel if there is risk of bleeding into a closed space, for example neurosurgery or posterior chamber eye surgery.

At ECNHS Trust we have no immediate on-site access to either platelets to treat clopidogrel-induced bleeding or prasugrel / ticagrelor induced bleeding, or PCI to treat stent thrombosis. It may be that patients where this balance is very controversial should have their surgery in institutions where these are available.

Type of stent and timing of insertion:
There are two main types of stent; bare metal stents and drug eluting stents.

Bare metal stents:
BMS fail by being occluded with scar tissue. The risk is 12-20% within six months. Late re-stenosis is rare. Clopidogrel is normally only given until the stent is epithelialised, which takes about 6-12 weeks. Stopping it after that time is probably low risk.

Drug eluting stents:
These are coated with an antiproliferative drug to prevent scarring. However, the drug elution prevents them epithelialising rendering them *more* prone to thrombosis, especially on stopping clopidogrel. DES fails by stent thrombosis. The risk is 5% within 6 months. Clopidogrel is therefore used for a year and the trend is to use it for even longer. 80% of stents inserted are now of this type.

With both types, aspirin therapy is usually for life.

The European Society of Cardiologists recommends that if it is known that the patient will have non-cardiac surgery soon, a BMS should be used.

Examples of possible scenarios:

1. Patient listed for elective knee replacement.

Serious consideration should be given to deferring the surgery until the clopidogrel or would normally have been stopped. This would not normally be for more than a year.

2. Patient requiring emergency surgery with a high risk of bleeding.

Order platelets as well as cross matching blood. Do not use a neuraxial block. Restart antiplatelet therapy as soon as team confident that risk of bleeding is low

3. Patient for an urgent planned laparotomy for colorectal cancer.

Potentially the most difficult because the timing of surgery is restricted. Anaesthetist will have to try to quantify how much of a survival benefit an epidural could afford, which will depend on how "high risk" the patient is. Many may have to be done with a PCA.
If the decision is to continue clopidogrel; platelets should be available in the hospital.

If clopidogrel or Ticagrelor is stopped:

aspirin should be continued.
the patient should have prophylactic LMWH (as per Trusts Venous Thromboembolism Prevention and Treatment Guidelines) once a day at night for three days afterwards
It should be restarted as soon as possible. This may be:
- the same day unless there is a reason not to
- as soon as the patient can eat and drink
- after an epidural catheter has been removed at 48-72 hours post-op.

An initial loading dose of 300mg of clopidogrel or 180mg of ticagrelor should be given.

In all cases, the decision about what to do with a stented patient's antiplatelet therapy should be discussed with them during the consent process.

References:

Review Article- Coronary artery stents and non-cardiac surgery
Howard-Alpe G, de Bono J et al
British Journal of Anaesthesia 98(5):560-574 (2007)

Editorial- Coronary stents and peri-operative anti-platelet regimen: dilemma of bleeding and stent thrombosis
Spahn D, Howell S et al
British Journal of Anaesthesia 96(6):675-677 (2006)

Coronary artery stenting and non-cardiac surgery- a prospective outcome study
Vicenzi M, Meislitzer T et al
British Journal of Anaesthesia 96(6):686-693 (2006)

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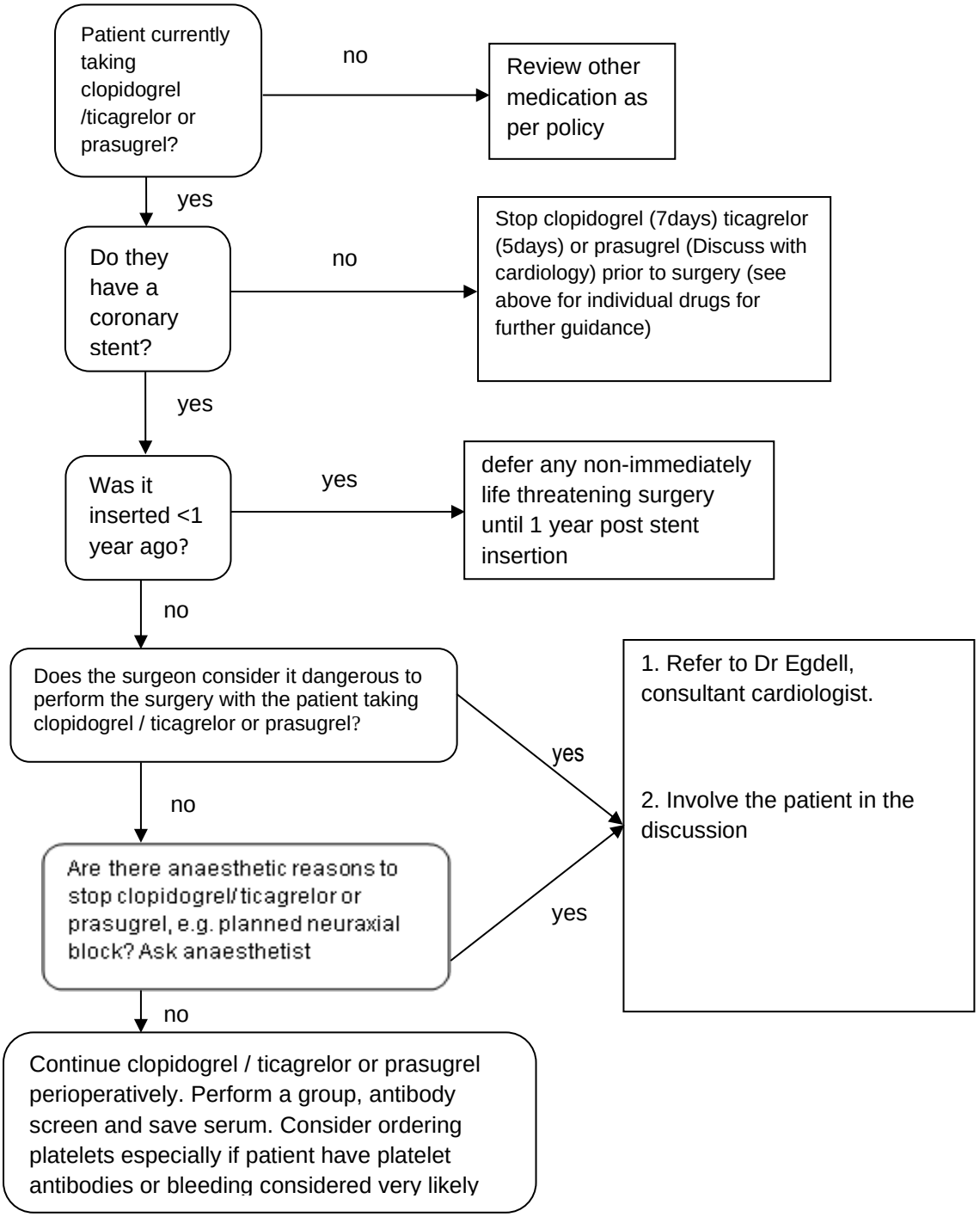
Flow chart for the management of clopidogrel / ticagrelor/prasugrel peri-operatively



The following is a guide for pre-operative assessment staff. At least at first, the decision in each case is going to be a very individual one. As patterns emerge and more information becomes available it may be possible for a chart like this to cover more eventualities.

Appendix 3:

Guideline for peri-operative adjustment of non-insulin medication

Tablets	Day prior to admission	Day of surgery / whilst on a VRIII		
		Patient for a.m. surgery	Patient for p.m. surgery	If a VRIII is being used*
Acarbose	Take as normal	Omit morning dose if NBM	Give morning dose if eating	Stop once VRIII commenced, do not recommence until eating and drinking normally
Meglitinide (repaglinide or nateglinide)	Take as normal	Omit morning dose if NBM	Give morning dose if eating	Stop once VRIII commenced, do not recommence until eating and drinking normally
Metformin (eGFR is greater than 60 ml/min/1.73m2 and procedure not requiring use of contrast media**)	Take as normal	If taken once or twice a day – take as normal If taken three times per day, omit lunchtime dose	If taken once or twice a day – take as normal If taken three times per day, omit lunchtime dose	Stop once VRIII commenced, do not recommence until eating and drinking normally
Sulphonylurea (e.g. glibenclamide, gliclazide, glipizide, glimeperide)	Take as normal	If taken once daily in the morning – omit the dose that day If taken twice daily – omit the morning dose that day	If taken once daily in the morning – omit the dose that day If taken twice daily – omit both doses that day	Stop once VRIII commenced, do not recommence until eating and drinking normally
Pioglitazone	Take as normal	Take as normal	Take as normal	Stop once VRIII commenced, do not recommence until eating and drinking normally
DPP IV inhibitor (e.g. sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin)	Take as normal	Take as normal	Take as normal	Stop once VRIII commenced, do not recommence until eating and drinking normally

Tablets	Day prior to admission	Day of surgery / whilst on a VRIII		
		Patient for a.m. surgery	**Patient for p.m. surgery**	**If a VRIII is being used***
GLP-1 analogue (e.g. exenatide, liraglutide, lixisenatide, dulaglutide)	Take as normal	Take as normal Please Note: post operatively the weekly GLP-1 analogue injection can be delayed upto 3 days	Take as normal Please Note: post operatively the weekly GLP-1 analogue injection can be delayed upto 3 days	Take as normal
SGLT-2 inhibitors (e.g. dapagliflozin, canagliflozin, ertugliflozin empagliflozin)	Omit day prior to surgery	Omit on day of surgery	Omit on day of surgery	Omit until eating and drinking normally

Please note

SGLT-2 inhibitors: Advice for healthcare professionals in secondary care

- **Sodium-glucose co-transporter (SGLT2) inhibitors available in the UK are canagliflozin, dapagliflozin, empagliflozin or ertugliflozin. For full prescribing details please see BNF or Summary of Product characteristics available at www.medicines.org.uk**
- **Due to their association with a risk of diabetic ketoacidosis (including euglycaemic ketoacidosis) the advice below for healthcare professionals has been issued so that patients who are at risk of developing (or are in the early stages of) diabetic ketoacidosis, can be identified and prompt corrective measures taken**
- **Monitor ketones during the peri operative period (every six hourly). Measurement of blood ketones is preferred to urine (monitor ketones when monitoring blood glucose)**
- **Restart the SGLT2 inhibitor once ketone values are normal, patient's condition has stabilised and is eating and drinking**
- **If patients cannot restart their SGLT2 inhibitors e.g. not absorbing ,abnormal ketone values and blood glucose needs to be controlled then seek advice from the endocrinologist**
- Report suspected adverse drug reactions to SGLT2 inhibitors via the Yellow Card Scheme
- **Please note that patient may require alternative treatment to maintain glycaemic control during their hospital stay, this is usually insulin. Please contact the diabetes team for advice on the management of these patients. Please ensure the SGLT2 inhibitor is reviewed to restart once the patient is stabilised and has normal ketone values, as SGLT2 inhibitors have long term benefits for adults with diabetes**

*If the patient requires and ongoing VRIII then the long acting background insulin should be continued but at 80% of the dose the patient usually takes when they are well. Normal insulin doses should be recommenced when the patient is eating and drinking normally.

At the pre-operative assessment clinic, all patients should have emergency treatment for hypoglycaemia written on their drug chart – i.e. Glucogel®, and 20% dextrose. Rapid acting Insulin should also be prescribed.

The management of perioperative hyperglycaemia and hypoglycaemia is outlined in Appendix 4.

Warn the patient that their blood glucose control may be erratic for a few days after the procedure.

NBM – Nil By Mouth, OD – Once Daily, BD – Twice Daily, TDS – Three times Daily, a.m. – morning, p.m. – afternoon

**** If contrast medium is to be used and eGFR less than 60ml/min/1.73m2, metformin should be omitted on the day of the procedure and for the following 48 hours**

If eGFR < 60ml/min but patient not having contrast medium – continue metformin as per >60mls/min above.

Appendix 4: Guideline for peri-operative adjustment of insulin

	Insulins	Example medications	Day prior to admission	Day of Surgery		Whilst on VRIII*
				a.m. surgery	p.m. surgery	
Long Acting Insulin	Once daily long acting (morning)	Abasaglar® Humulin I® Insulatard ® Insuman Basal® Lantus® Levemir® Semglee® Tresiba® Toujeo® Xultophy®	No Dose adjustment necessary	**Reduce dose by 20%** Check blood glucose on admission	**Reduce dose by 20%** Check blood glucose on admission	Continue at 80% of the usual dose
	Once daily long acting (Lunchtime)		**Reduce dose by 20%**	Restart insulin at normal dose when eating and drinking starts	Restart insulin at normal dose when eating and drinking starts	Continue at 80% of the usual dose
	Once daily long acting (evening)		**Reduce dose by 20%**	No dose adjustment Necessary	No dose Adjustment Necessary	Continue at 80% of the usual dose
	Twice daily long acting insulin		No change to morning dose, **evening dose needs to be reduced by 20%**	Morning dose needs to be **reduced by 20%** Check blood glucose on admission No change to patients usual Evening dose	Morning dose needs to be **reduced by 20%** Check blood glucose on admission No change to patients usual Evening dose	Continue at 80% of the usual dose

Due to the potential for insulin preparations to change, this table is for guidance only and reference should be made to the UKCPA Handbook of Perioperative Medicines for up-to-date information

	Insulins	Example medications	Day prior to admission	Day of Surgery		Whilst on VRIII*
				a.m. surgery	p.m. surgery	
Short acting Insulin	**Short Acting insulin with meals (two to four doses a day)**	Actrapid® NovoRapid® Apidra® Fiasp® Humalog® Humulin S® Hypurin® Porcine Neutral Insuman rapid® Lyumjev®	No Dose adjustment necessary	Omit morning dose if no breakfast is eaten Check blood glucose on admission **Omit** lunchtime dose if not eating and drinking normally Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose.	Take usual morning insulin dose with breakfast **Omit** lunchtime dose if not eating. Check blood glucose on admission Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose.	Not needed whilst on VRIII

	Insulins	Example medications	Day prior to admission	Day of Surgery		Whilst on VRIII*
				a.m surgery	p.m surgery	
Premixed Insulin prepared by manufacturers	Twice daily	Novomix 30® Humulin M3® Humalog Mix 25® Humalog Mix 50® Hypurin Porcine (30/70 Mix®) Insuman Comb 15® Insuman Comb 25® Insuman Comb 50®	No Dose adjustment necessary	**Halve usual morning dose** Check blood glucose on admission Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give half usual dose.	**Halve usual morning dose** Check blood glucose on admission Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose.	Not needed whilst on VRIII
	Three times a day		No Dose adjustment necessary	**Halve usual morning dose** Check blood glucose on admission **Omit** Lunchtime dose Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose.	**Halve usual morning dose** Check blood glucose on admission **Omit** Lunchtime dose Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose.	Not needed whilst on VRIII

	Insulins	Example medications	Day prior to admission	Day of Surgery		Whilst on VRIII*
				a.m surgery	p.m surgery	
Self-mixed Insulin prepared by patient/carer	Twice daily (two different types of insulin combined by the person with diabetes into one injection)	**Short Acting:** Actrapid® NovoRapid® Apidra® Fiasp® Humalog® Humulin S® Hypurin® Porcine Neutral Insuman rapid® Lyumjev® **AND** **Intermediate acting:** Humulin I® Hypurin® Porcine Isophane Insulatard®	No Dose adjustment necessary	Calculate the total dose of both morning insulin and **give half of this total dose** as intermediate acting insulin only, in the morning. Check blood glucose on admission Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose. If not eating give basal only component of the usual mixed insulin.	Calculate the total dose of both morning insulin and **give half of this total dose** as intermediate acting insulin only, in the morning. Check blood glucose on admission Resume normal insulin with evening meal if eating a normal meal. If eating a half/small meal give **half** usual dose. If not eating give basal only component of the usual mixed insulin.	Not needed whilst on VRIII

*If the patient requires ongoing VRIII, then the long-acting background insulin should be continued but at 80% of the usual dose the patient takes when they are well. Normal insulin doses should be recommended when the patient is eating and drinking normally.

On admission, all patients should have emergency treatment for hypoglycaemia written on their drug chart i.e Glucogel ®, 20% dextrose. Rapid acting insulin should also be prescribed. See Appendix 4 of "**Inpatient management of Hypoglycaemia in adults with Diabetes Mellitus**" Click here. **Warn the patient their blood glucose control may be erratic for a few days after the procedure.**

Appendix 5

Criteria for patients receiving exogenous glucocorticoids who need pre- and post-operative steroid cover

(For guidance of steroid cover required - see Appendix 6)

Criteria for patients who need pre- and post-operative steroid cover:

1. Patients with **Addison's disease**
2. Patients who have received a **long-term course of glucocorticoids** (more than 4 weeks) within the last 12 months i.e Prednisolone ≥ 5mg od (see Table 1 for equivalent doses)
3. Patients who have received **3 or more short courses of high-dose oral glucocorticoids** within the last 12 months (see Table 2)
4. **Repeated courses of dexamethasone as an antiemetic in oncology regimens**, and for 12 months after stopping
5. **Prolonged courses of dexamethasone for the treatment of severe Covid-19** (>10 days)
6. **High dose inhaled steroids** >1000mcg/day beclomethasone or >500mcg/day fluticasone (or equivalent dose of another glucocorticoid), and for 12 months after stopping (See Table 3)
7. **High-dose (>/= 200g/ week) topical** potent or very potent glucocorticoids used across a large area of skin for 4 weeks or more, or factors increasing absorption assessed on a case-by-case basis, and for 12 months after stopping. (See Table 4)

Table 1: Long-term oral glucocorticoids (ie 4 weeks or longer)

Medicine	Dose (*)
Beclometasone	625 microgram per day or more
Betamethasone	750 microgram per day or more
Budesonide	1.5mg per day or more (***)
Deflazacort	6mg per day or more
Dexamethasone	500 microgram per day or more (**)
Hydrocortisone	15mg per day or more (**)
Methylprednisolone	4mg per day or more
Prednisone	5mg per day or more
Prednisolone	5mg per day or more

(*) dose equivalent from BNF except (**) where dose reflects that described in the guideline by Simpson et al (2020) and (***) based on best estimate.

Table 2: Short-term oral glucocorticoids (one week course or longer and has been on long-term course within the last year or has regular need for repeated courses)

Medicine	Dose (*)
Beclometasone	5mg
Betamethasone	6mg per day or more
Budesonide	12mg (***)
Deflazacort	48mg per day or more
Dexamethasone	4mg per day or more (**)
Hydrocortisone	120mg per day or more (**)
Methylprednisolone	32mg per day or more
Prednisone	40mg per day or more
Prednisolone	40mg per day or more

(*) dose equivalent from BNF except (**) where dose reflects that given associated Guidance (Simpson et al 2020) and (***) based on best estimate

Table 3: Doses of inhaled corticosteroids in adults that require consideration of giving peri-operative steroid cover (Adapted from Guidance developed by London Respiratory Network)

Inhaled Corticosteroid	Total Daily Dose of inhaled Corticosteroid		
	Low dose No Peri-operative steroid cover required	**Peri-operative steroid cover to be given if patient also using nasal/topical preps with steroid inhalers**	**Peri-operative steroid cover required**
Pressurised metered dose inhalers (pMDI)			
Beclometasone dipropionate			
Non-proprietary	100 micrograms two puffs twice a day	200 micrograms two puffs twice a day	200 micrograms four puffs twice a day
Clenil Modulite pMDI	100 micrograms two puffs twice a day	200 micrograms two puffs twice a day 250 micrograms two puffs twice a day	250 micrograms four puffs twice a day
Kelhale pMDI (extrafine)	50 micrograms two puffs twice a day	100 micrograms two puffs twice a day	100 micrograms four puffs twice a day
Qvar pMDI (extrafine), Qvar Autohaler (extrafine) & Qvar Easi-breathe (extrafine)	50 micrograms two puffs twice a day	100 micrograms two puffs twice a day	100 micrograms four puffs twice a day
Soprobec pMDI	100 micrograms two puffs twice a day	200 micrograms two puffs twice a day 250 micrograms two puffs twice a day	250 micrograms four puffs twice a day
Ciclesonide			
Alvesco pMDI	80 micrograms two puffs once a day	160 micrograms two puffs once a day	160 micrograms two puffs twice a day
Fluticasone propionate			
Flixotide Evohaler	50 micrograms two puffs twice a day	125 micrograms two puffs twice a day	250 micrograms two puffs twice a day
Dry powder inhalers (DPI)			
Beclometasone			
Non-proprietary Easyhaler	200 micrograms one puff twice a day	200 micrograms two puffs twice a day	
Budesonide			
Non-proprietary Easyhaler	100 micrograms two puffs twice a day	200 micrograms two puffs twice a day	400 micrograms two puffs twice a day
Budelin Novolizer		200 micrograms two puffs twice a day	200 micrograms four puffs twice a day
Pulmicort Turbohaler	100 micrograms two puffs twice a day 200 micrograms one puff twice a day	200 micrograms two puffs twice a day 400 micrograms one puff twice a day	400 micrograms two puffs twice a day
Fluticasone propionate			
Flixotide Accuhaler	100 micrograms one puffs twice a day	250 micrograms one puff twice a day	500 micrograms one puff twice a day

Inhaled Corticosteroid	Total Daily Dose of Inhaled Corticosteroid		
	Low dose No Peri-operative steroid cover required	**Peri-operative steroid cover to be given if patient also using nasal/topical preps with steroid inhalers**	**Peri-operative steroid cover required**
Mometasone			
Asmanex Twisthaler		200 micrograms one puff twice a day	400 micrograms one puff twice a day
Combination inhalers			
Beclometasone dipropionate (extrafine) with formoterol			
Fostair (pMDI)	100/6 one puff twice daily	100/6 two puffs twice daily	200/6 two puffs twice daily
Fostair (NEXThaler)	100/6 one puff twice daily	100/6 two puffs twice daily	200/6 two puffs twice daily
Luforbec	100/6 one puffs twice a day	100/6 two puff twice a day	200/6 two puffs twice daily
Beclometasone, formotorol with glycopyrronium			
Trimbow (pMDI)	n/a	87/5/9 two puffs twice daily	172/5/9 two puffs twice a day
Trimbow NEXThaler	n/a	88/5/9 two puffs twice a day	n/a
Budesonide with formoterol			
DuoResp Spiromax	160/4.5 one puff twice daily	160/4.5 two puffs twice daily 320/9 one puff twice daily	320/9 two puffs twice daily
Symbicort Turbohaler	100/6 two puffs twice daily 200/6 one puff twice daily	200/6 two puffs twice daily 400/12 one puff twice daily	400/12 two puffs twice daily
Symbicort pMDI	100/3 two puffs twice daily	100/3 four puffs twice daily 200/6 two puffs daily	200/6 four puffs twice daily
Fobumix Easyhaler	80/4.5 two puffs twice a day 160/4.5 one puff twice a day	160/4.5 two puffs twice a day 320/9 one puff twice a day	320/9 two puffs twice a day
WockAIR	160/4.5 one puff twice daily	160/4.5 two puffs twice daily 320/9 one puffs twice daily	320/9 two puffs twice daily
Budesonide, formoterol with Glycopyrronium			
Trixeo Aerosphere	n/a	160/5/7.2 two puffs twice daily	n/a
Fluticasone propionate with formoterol			
Flutiform MDI	50/5 two puffs twice daily	125/5 two puffs twice daily	250/10 two puffs twice a day
Flutiform K-haler	50/5 two puffs twice daily	125/5 two puffs twice daily	n/a
Fluticasone propionate with salmeterol			
AirFluSal Forspiro	n/a	n/a	500/50 one puff twice a day
AirFluSal pMDI	n/a	125/25 two puffs twice a day	250/25 two puffs twice a day
Aloflute pMDI	n/a	125/25 two puffs twice a day	250/25 two puffs twice a day
Avenor pMDI	50/25 two puffs twice a day	125/25 two puffs twice a day	250/25 two puffs twice a day
Combisal pMDI	50/25 two puffs twice a day	125/25 two puffs twice a day	250/25 two puffs twice a day
Fixkoh Airmaster	100/50 one puff twice daily	250/50 one puff twice daily	500/50 one puff twice daily
Fusacomb Easyhaler	n/a	250/50 one puff twice a day	500/50 one puff twice a day

Inhaled Corticosteroid	Total Daily Dose of Inhaled Corticosteroid		
	Low dose No Peri-operative steroid cover required	Peri-operative steroid cover to be given if patient also using nasal/topical preps with steroid inhalers	Peri-operative steroid cover required
Fluticasone propionate with salmeterol (continued)			
Seffalair spiromax	100/12.75 one puff twice daily	202/12.75 one puff twice daily	
Sereflo pMDI	n/a	125/25 two puffs twice a day	250/25 two puffs twice a day
Sereflo ciphaler	n/a	250/50 one puff once daily	
Seretide Accuhaler	100/50 one puff twice daily	250/50 one puff twice daily	500/50 one puff twice daily
Seretide Evohaler	50/25 two puffs twice a day	125/25 two puffs twice a day	250/25 two puffs twice a day
Sirdupla pMDI	n/a	125/25 two puffs twice a day	250/25 two puffs twice a day
Stalpex	n/a	n/a	500/50 one puff twice daily
Fluticasone furoate with vilanterol			
Relvar Ellipta	n/a	92/22 one puff once a day	184/22 one puff once a day
Fluticasone furoate with vilanterol and umeclidinium			
Trelegy Ellipta	n/a	92/22/55 one puff once daily	n/a
Mometasone furoate with indacaterol			
Atectura Breezhaler	62.5/125 one puff once daily	127.5/125 one puff once daily	260/125 one puff once daily
Fluticasone furoate, glycopyrronium and indacaterol			
Enerzair Breezhaler		136/46/114 one puff once daily	

Table 4: Topical glucocorticoids

Topical steroid treatments	Potency of steroid
Beclometasone dipropionate 0.025%	Potent
Betamethasone dipropionate 0.05% and higher [incl Dalonev, Diprosone, Dovobet, Enstilar, in combination with clotrimazole (incl Lotriderm) and salicylic acid (incl Diprosalic)]	Potent
Betamethasone valerate 0.1% and higher [incl Audovate, Betacap, Betesil, Betnovate, Bettamousse, and in combination with clioquinol, fusidic acid (incl Fucibet, Xemacort) or neomycin]	Potent
Clobetasol propionate 0.05% and higher [incl. Clarelux, ClobaDerm, Dermovate, Etrivex and in combination with neomycin and nystatin]	Very potent
Diflucortolone valerate 0.1% [incl Nerisone]	Potent
Diflucortolone valerate 0.3% [incl Nerisone Forte]	Very Potent
Fluocinonide 0.05% [incl Metosyn]	Potent
Fluocinolone acetonide 0.025% [(incl. Synalar) and in combination with clioquinol (incl Synalar C)]	Potent
Fluticasone propionate 0.05% [incl Cutivate]	Potent
Hydrocortisone butyrate 0.1% [incl Locoid]	Potent
Mometasone 0.1% [incl Elocon]	Potent
Triamcinolone acetonide 0.1% [incl Aureocort]	Potent

Appendix 6: Surgical Guidelines for Management of steroid dependant patients

References: Surgical Guidelines for Addison's disease and other forms of adrenal insufficiency patients requiring continuous steroid cover. Addison's Clinical Advisory Panel. Jan 2021 & Anaesthesia 2020, 75, 654-663

TYPE OF PROCEDURE	PRE-OPERATIVE AND OPERATIVE NEEDS *(See Notes 1, 2)*	POST-OPERATIVE NEEDS *(See Notes 6, 8, 9)*
LENGTHY, MAJOR SURGERY WITH LONG RECOVERY TIME *eg. open heart surgery, major bowel surgery,*	100mg hydrocortisone IM or IV just before anaesthesia. *(See Notes 2, 3, 7)* Immediately followed by 100mg IM or IV 6 hourly	100mg IM or IV every 6 hours *(See Notes 3, 5)* or until able to eat & drink normally *(discharged from ITU)* If well, then double oral dose for 48+ hours. *(See Note 14)* Then taper the return to normal dose
MAJOR SURGERY WITH RAPID RECOVERY *eg. caesarean section, joint replacement*	100mg hydrocortisone IM or IV just before anaesthesia. *(See Notes 2, 6, 7)* Immediately followed by 100mg IM or IV 6 hourly	100mg IM or IV every 6 hours *(See Notes 3, 5)* for 24 - 48 hours *(or until able to eat and drink normally)* If well, then double oral dose for 24 - 48 hours. *(See Note 14)* Then return to normal dose
LABOUR AND VAGINAL BIRTH	100mg hydrocortisone IM or IV at onset of active labour. *(See Note 4-7)* Immediately followed by 50mg IM or IV 6 hourly until delivery	Double oral dose for 24 - 48 hours after delivery. *(See Note 14)* If well, then return to normal dose
MINOR SURGERY *eg. cataract surgery, hernia repairs, laparoscopy with local anaesthetic*	100mg hydrocortisone IM just before anaesthesia *(See Note 6)*	Double oral dose for 24 hours. *(See Note 14)* Then return to normal dose
MINOR PROCEDURE *eg. skin mole removal with local anaesthetic*	Take an extra oral dose, 60 minutes ahead of the procedure	An extra dose 60 minutes after the procedure. *(See Note 14)* Then return to normal dose
INVASIVE BOWEL PROCEDURES REQUIRING LAXATIVES *eg. colonoscopy, barium enema*	Hospital admission overnight with IV fluids and 100mg hydrocortisone IM during preparation. *(See Notes 3, 5, 6)* 100mg hydrocortisone IM at commencement *(See Notes 1, 6)*	Double dose oral medication for 24 hours. *(See Note 14)* Then return to normal dose
OTHER INVASIVE PROCEDURES *eg. endoscopy, gastroscopy*	100mg hydrocortisone IM just before commencing	Double dose oral medication for 24 hours. *(See Note 14)*. Then return to normal dose
MAJOR DENTAL SURGERY *eg. dental extraction/s with local or general anaesthetic*	100mg hydrocortisone IM just before anaesthesia *(See Notes 6, 7, 8)*	Double dose oral medication for 24 hours. *(See Note 14)* Then return to normal dose
DENTAL SURGERY *eg. root canal work with local anaesthetic*	Double oral dose *(up to 20mg hydrocortisone)* one hour prior to surgery	Double dose oral medication for 24 hours. *(See Note 14)* Then return to normal dose
MINOR DENTAL PROCEDURE *eg. replace filling, scale and polish*	Take an extra oral dose, 60 minutes ahead of the procedure	An extra dose where hypoadrenal symptoms occur afterwards. *(See Note 14)* Then return to normal dose

NOTES

1. Give the steroid-dependent patient first-on-the-list status (alongside insulin-dependent diabetes) to minimise the risks of dehydration.
2. For any nil-by-mouth regimen, arrange an intravenous saline infusion (0.9% saline or equivalent) to prevent dehydration and maintain mineral corticoid stability, eg. 1000ml every 8 hours if >50kg.
3. Continuous IV hydrocortisone infusion is preferable to 6 hourly IM or IV injection as it gives more stable cover. Arrange as 100mg bolus followed by 8.33mg per hour or 200mg per 24 hours.
4. Active labour is cervical dilation >4cm.
5. Arrange continuous IV infusion cover for steroid-dependent patients taking CYP3A4 accelerants, eg. anticonvulsants, rifampicin and antifungal drugs, to minimise the risk of decompensation.
6. IM hydrocortisone is preferable to IV injection for its more sustained duration.
7. Administer bolus hydrocortisone over a minimum of 10 minutes to prevent vascular damage.
8. Hydrocortisone acetate cannot be used due to its slow-release, microcrystalline formulation. Ensure parenteral drug is hydrocortisone sodium phosphate or hydrocortisone sodium succinate, 100mg.
9. Monitor electrolytes and blood pressure post-operatively for all procedures requiring parenteral steroid cover. If the patient becomes hypotensive, drowsy or peripherally shut down, administer 100mg hydrocortisone IV or IM bolus immediately.
10. If any post-operative complications arise, eg. fever, delay the return to normal dose.
11. Ensure back-up supplies of oral and injectable hydrocortisone are available for resuscitation before commencing surgery. Even at full steroid cover, post-operative resuscitation may occasionally be required.
12. A pre-assessment meeting with the anaesthetist is advisable for all steroid-dependent patients, to ensure any comorbidities and potential drug interactions are taken into account.
13. Patients who have been taking 5mg prednisolone or more long-term should be regarded as potentially suppressed and managed with perioperative supplemental steroid cover, on a precautionary basis.
14. Double dose only for prednisolone, hydrocortisone, dexamethasone, methylprednisolone. Check individual Summary of Product Characteristics.

Appendix 7

Herbal Medicines with potential peri-operative complications

Disclaimer:

This guideline is believed to be an accurate reflection of the most current evidenced based literature available at time of composition. This is not an exhaustive list; it is intended to be used as a guide only. Users are advised to always consult medical literature and take into account any new developments. Always relate the information provided to the individual clinical situation.

Background:

The use of natural medicines in the UK is extensive. Many patients do not consider these products to be drugs or medication and often do not disclose their use to health providers. As a result there is a risk that patients may take these products in the perioperative period without healthcare provider's knowledge.

Purpose:

Many natural medicines have pharmacological effects that have the potential to interfere with surgical procedures. Therefore, assessment of natural medicine use is an important aspect of perioperative assessment. Patients should be asked specifically about their use of herbs, vitamins, minerals, or other natural or alternative products.

Advise patients to discontinue taking all non-essential natural medicines two weeks before an elective surgery procedure. Some products may not need to be discontinued this far in advance; however, there often is not enough information about which constituents cause a particular pharmacological effect or the half-life of those constituents.

Below is a list of herbal medicines known to have pharmacological effects which could adversely affect surgery**. If a patient discloses a medication not on this list but wishes to continue taking it, please seek further advice from pharmacy.**

Constituent	Reason why it should be stopped
5-HTP	Has serotonergic properties; treat as an SSRI. Caution with pethidine use.
Agnus Castus	Pro-oestrogenic; could increase thrombus risk Dopamine agonist; Treat as haloperidol clozapine or sulpiride.
Agrimony	Clinical evidence of hypotensive effects Clinical research suggests hypoglycaemic effects
Alfalfa	Immunomodulating properties; Possible increased risk of infection and poor wound healing Pro-oestrogenic; could increase thrombus risk Clinical research suggests hypoglycaemic effects

Aloes/Aloe vera	Clinical research suggests hypoglycaemic effects
Alpha-lipoic acid	Clinical research suggests hypoglycaemic effects
Andrographis	Preliminary evidence of hypotensive effects
Aniseed	Pro-oestrogenic; could increase thrombus risk Sympathomimetic; can cause hypertension, tachycardia and arrythmias
Arnica	Anticholinesterase action; bradycardia, hypotension, bronchoconstriction.
Asafoetida	Clinical evidence of hypotensive effects
Avens	Clinical evidence of hypotensive effects
Banaba	Clinical research suggests hypoglycaemic effects
Bayberry	Mineralocorticoid effect; could increase blood pressure
Bilberry	Antiplatelet effect; increases bleeding risk
Bitter melon	Clinical research suggests hypoglycaemic effects
Bitter orange	Stimulant. Structurally related to phenylephrine, it can predispose the patient to stroke, myocardial infarction, arrhythmia from tachycardia and hypertension. May interact with MAOIs. Omit a minimum of 24hours pre-op.
Black Cohosh	Pro-oestrogenic; could increase thrombus risk
Black tea (concentrated tablets)	Large quantities of caffeine in black tea can have antiplatelet effects; increased bleeding risk
Blue Cohosh	Theoretical hypertensive effects
Boldo	Anticoagulation effect; increased risk of bleeding. Can potentiate the effects of warfarin.
Boneset	Immunomodulating properties; Possible increased risk of infection and poor wound healing
Broom	Hypertensive; potential to raise blood pressure Potential cardiac depressant activity
Burdock	Clinical research suggests hypoglycaemic effects

Butterbur	Clinical evidence of hypotensive effects
Calamus	Clinical evidence of hypotensive effects Theoretical catecholamine activity Potentiates barbiturate sleeping time
Calendula	Immunomodulating properties; Possible increased risk of infection and poor wound healing
Capsicum	Sympathomimetic; can cause hypertension, tachycardia and arrhythmias
Cat's Claw	Antiplatelet effect; increases bleeding risk Clinical evidence of hypotensive effects Immunomodulating properties; Possible increased risk of infection and poor wound healing
Celery	Clinical research suggests hypoglycaemic effects Sedatives effect
Centaury	Sedative effect
Chamomile	Immunomodulating properties; Possible increased risk of infection and poor wound healing Mild sedative effects; could potentiate anaesthetics
Chondroitin	Anticoagulation effect; increased risk of bleeding. Can potentiate the effects of warfarin. Chondroitin also affects blood sugar control
Clove	Antiplatelet effect; increases bleeding risk
Coenzyme Q10	Clinical research suggesting modest hypotensive effects
Cola nut	Stimulant. Increased risk of tachycardia and hypertension.
Coltsfoot	Vasopressor activity causes hypertension
Corn Silk	Clinical evidence of hypotensive effects Clinical research suggests hypoglycaemic effects
Couchgrass	Sedative effect
Cowslip	Initially causes hypotension, then later hypertension
Damiana	Clinical research suggests hypoglycaemic effects
Dandelion	Clinical research suggests hypoglycaemic effects
Danshen	Anticoagulation effect; increased risk of bleeding. Can potentiate the effects of warfarin
Devil's Claw	Clinical research suggests hypoglycaemic effects Clinical evidence of hypotensive effects
Dong quai	Anticoagulation effect; increased risk of bleeding. Can potentiate the effects of warfarin

Drosera	Immunomodulating properties; Possible increased risk of infection and poor wound healing
Echinacea	Possible increased risk of infection and poor wound healing
Elecampane	Clinical research suggests hypoglycaemic effects Sedative effect Clinical evidence of hypotensive effects
Ephedra	Stimulant: Is a source of ephedrine, pseudoephedrine, and phenylpropanolamine. Can cause tachycardia and hypertension with spontaneous adverse events including stroke, myocardial infarction, QT interval prolongation and arrhythmia. Also known to inhibit complement pathway
Epimedium	Preliminary evidence of hypotensive effects
Eucalyptus	Clinical research suggests hypoglycaemic effects
Fenugreek	Anticholinesterase action; bradycardia, hypotension, bronchoconstriction. Anticoagulation effect; increased risk of bleeding. Can potentiate the effects of warfarin Clinical research suggests hypoglycaemic effects
Feverfew	Antiplatelet effect; increases bleeding risk
Fucus	Anticoagulation effect; increased risk of bleeding. Potential hypotensive effects Both hyper- and hypo thyroidism reported with continued use
Fumitory	Clinical evidence of hypotensive effects
Garlic	Antiplatelet effect; increases bleeding risk Also has hypotensive properties Clinical research suggests hypoglycaemic effects
Ginger	Antiplatelet effect; increases bleeding risk Clinical research suggests hypoglycaemic effects Also has hypotensive properties
Ginkgo	Pro-oestrogenic; could increase thrombus risk MAOI activity Antiplatelet effect; increases bleeding risk
Ginseng (American, Eleutherococcus and Panax)	Immunomodulating properties; Possible increased risk of infection and poor wound healing Has erratic blood glucose control in patients reporting both hyper- and hypo-glycaemic control CNS depressant and stimulant Pro-oestrogenic; could increase thrombus risk Antiplatelet effects; increases bleeding risk Also has erratic blood pressure altering properties, causing both hyper- and hypo-tension in patients. MAOI potentiation, suspected phenelzine interaction
Glucomannan	Clinical research suggesting hypoglycaemic effects
Glucosamine	Anticoagulation effect; increased risk of bleeding. Can potentiate the effects of warfarin. Glucosamine can also affect blood sugar control.
Golden Seal	Potential hypotensive effects Heparin antagonist Sedative effect
Greater Celandine	Immunomodulating properties; Possible increased risk of

	infection and poor wound healing
Green tea (concentrated)	Large quantities of caffeine in green tea can have antiplatelet effects; increased bleeding risk. It can also be a stimulant in large quantities.
Guarana	Antiplatelet effects; increases bleeding risk Also a known stimulant; increases risk of tachycardia, hypertension and arrhythmias.
Gymnema	Clinical research suggests hypoglycaemic effects
Hawthorn	Clinical evidence of hypotensive effects CNS depressant; potentiates barbiturate sleeping time
Hops	Mild sedative effects (usually used in combination with other sedative products). Could potentiate anaesthetics.
Horehound, White	Vasodilator properties; lowers blood pressure
Horse chestnut	Active constituents thought to have antiplatelet activity; increases bleeding risk. Clinical evidence of hypotensive effects
Horseradish	Clinical evidence of hypotensive effects Peroxidase stimulates synthesis of arachidonic acid metabolites Both hyper- and hypo thyroidism reported with continued use
Hydrocotyl	Hyperglycaemic effect Sedative effect
Jamaica Dogwood	Sedative effect
Java Tea	Clinical evidence of hypotensive effects Clinical research suggests hypoglycaemic effects
Juniper	Clinical evidence of hypotensive effects Clinical research suggests hypoglycaemic effects
Kava	Additive effects with benzodiazepines increasing sedation; also linked to numerous reports of hepatotoxicity Possible dopamine antagonist effects. Treat as haloperidol clozapine or sulpiride.
L-arginine	Clinical research suggesting modest hypotensive effects
Lavender	Mild sedative effects; additive effects with CNS depressants and anaesthetics.
Lemon balm	Clinical research suggesting sedative effects. Could potentiate anaesthetics.
Liquorice	Mineralocorticoid effect; could increase blood pressure Pro-oestrogenic; could increase thrombus risk Antiplatelet effect; increases bleeding risk Also has a laxative effect similar to senna. Particularly important to withdraw prior to bowel surgery.
L-tryptophan	Clinical research showing sedative effects; documented reports of additive effects with CNS depressants and anaesthetics. Also has serotinergic properties; treat as an SSRI. Caution with pethidine.
Marshmallow	Clinical research suggests hypoglycaemic effects
Maté	Stimulant. Increased risk of tachycardia and hypertension
Melatonin	Clinical research suggesting sedative effects; can potentiate anaesthetics. Seek anaesthetic advice if prescribed by a clinician (especially in children).
Mistletoe	Clinical evidence of hypotensive effects Promotes coagulation

	Immunomodulating properties; Possible increased risk of infection and poor wound healing
Motherwort	Oxytocic properties
Myrrh	Clinical research suggests hypoglycaemic effects
Nettle	Clinical evidence of hypotensive effects CNS depression, in vivo Clinical research suggests hypoglycaemic effects Anticholinesterase action; bradycardia, hypotension, bronchoconstriction.
Parsley	Sympathomimetic; can cause hypertension, tachycardia and arrhythmias
Passionflower	Mild sedative effects; animal models suggest additive effects with CNS depressants
Plantain	Clinical evidence of hypotensive effects
Pleurisy Root	Sympathomimetic; can cause hypertension, tachycardia and arrhythmias Pro-oestrogenic; could increase thrombus risk
Pokeroot	Clinical evidence of hypotensive effects
Policosanol	Possible antiplatelet effect (based on anecdotal evidence). May increase bleeding risk
Prickly Ash (North and South)	Clinical evidence of hypotensive effects
Prickly pear cactus	Clinical research suggesting hypoglycaemic effects
Red Clover	Pro-oestrogenic; could increase thrombus risk
Resveratrol	Possible antiplatelet effect (based on in vitro data). May increase bleeding risk
Rosemary	Hyperglycaemic effect
Sage	Potential hypotensive effects Sedative effect Clinical research suggests hypoglycaemic effects
SAMe,	Has serotinergic properties; treat as an SSRI. Caution with pethidine use.
Saw Palmetto	Immunomodulating properties; Possible increased risk of infection and poor wound healing. Both oestrogenic and anti-androgenic properties Possible antiplatelet effect (based on anecdotal evidence). May increase bleeding risk
Scullcap	Reputed action
Senega	CNS depressant, Clinical research suggests hypoglycaemic effects
Shepherd's Purse	Potentiates barbiturate sleeping time Anticholinesterase action; bradycardia, hypotension, bronchoconstriction.
Squill	Clinical evidence of hypotensive effects
St. John's wort	Has serotinergic properties; treat as an SSRI. Caution with pethidine use. Also reduces warfarin effect. Clinical evidence of hypotensive effects
Tansy	Clinical research suggests hypoglycaemic effects

Theanine	Hypotensive effects
Thyme	Clinical evidence of hypotensive effects
Valerian	Sedative effects. Potentiates anaesthetics. Advise patients to withdraw slowly to avoid withdrawal effects.
Vanadium	Clinical research suggesting hypoglycaemic effects
Vervain	Erratic blood pressure altering properties, causing both hyper- and hypo-tension in patients. Inhibition of gonadotrophic activity; conflicting results Some sympathomimetic activity; causing, tachycardia and arrhythmias
Vitamin E	High doses associated with antiplatelet effects; increases bleeding risk
Wild Carrot	Clinical evidence of hypotensive effects Sedative effect Pro-oestrogenic; could increase thrombus risk
Wild Lettuce	Sedative effect
Yarrow	Clinical evidence of hypotensive effects. Promotes coagulation

Appendix 8

Peri-operative guidance for anticoagulation (non- NOAC) , NOAC's and antiplatelet management for patients undergoing high risk therapeutic endoscopy procedures

Please see VTE guidelines Appendix 5 .Click here (Guidelines for the prevention and treatment of venous thromboembolism (VTE) in medical and surgical patients)

Perioperative Guidance for New Oral Anticoagulants (NOAC's) management undergoing high risk therapeutic endoscopy procedures

The following guidance has been adapted from the Handbook of Perioperative Medicines Aug 2016 developed by the United Kingdom Clinical Pharmacy Association

The European Heart Rhythm Association recommends that DOAC's can be stopped 24 hours before procedures that do not have clinically important bleeding risk e.g. ophthalmological and superficial dermatological procedures. For moderate and major endoscopic interventions it is recommended that DOAC's are stopped during the peri-operative period, as there is a lack of evidence for the safety of endoscopy while on these agents. Each DOAC has a different half-life which is extended in worsening renal impairment, please see below for drug specific guidance.

The endoscopist will indicate on the elective booking form whether the endoscopy procedure carries a high or low risk of bleeding, at the time of listing the patient for endoscopy.

Low bleeding risk procedure: Diagnostic endoscopy + biopsy, biliary stenting, pancreatic stenting, banding of haemorrhoids.

High bleeding risk procedure:

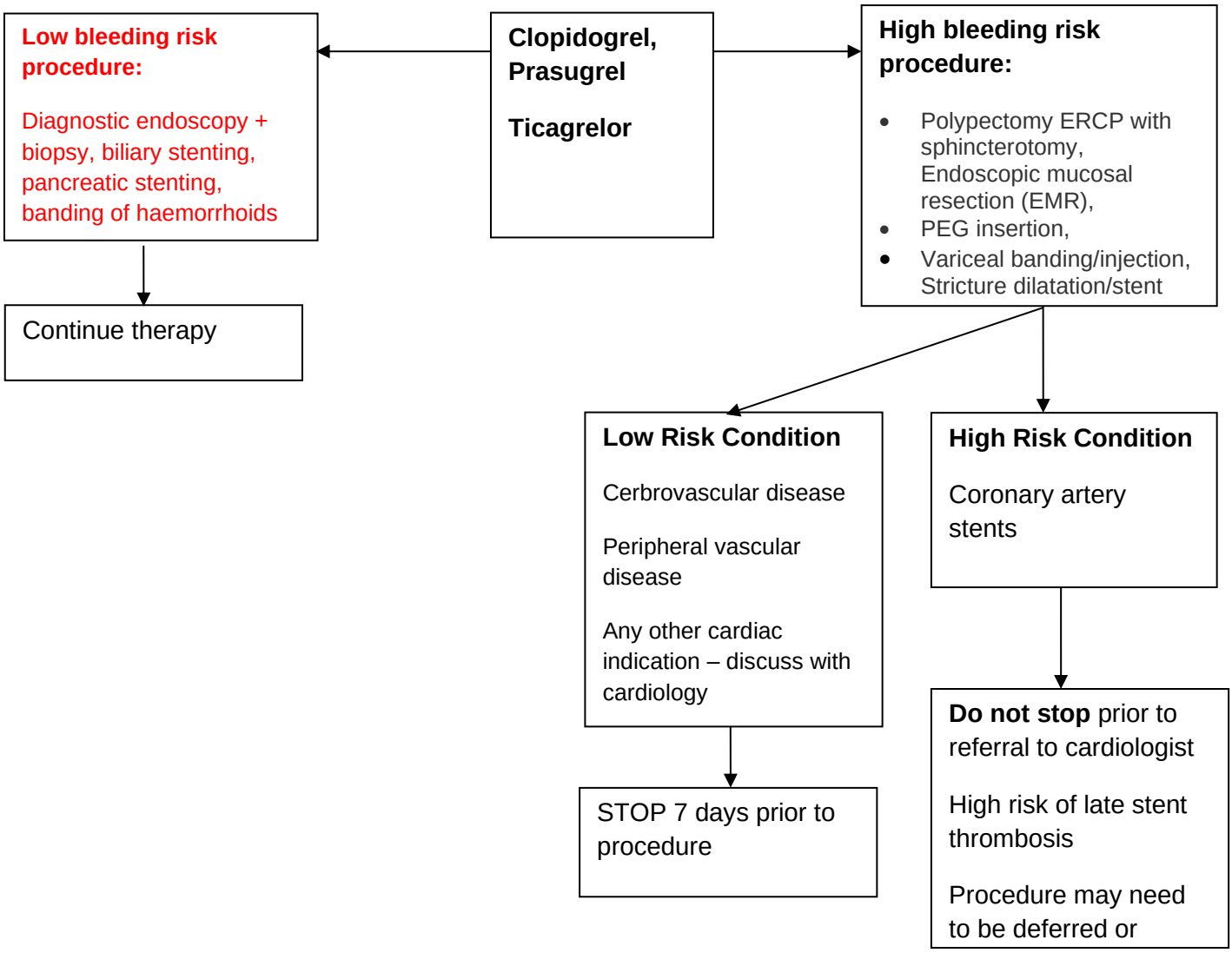
Polypectomy ERCP with sphincterotomy, endoscopic mucosal resection (EMR), PEG insertion, variceal

DOAC	Renal Function*	Procedure with low bleeding risk 12-25% residual anticoagulant effect at time of endoscopy acceptable	Procedure with high bleeding risk <10% residual anticoagulant effect at time of endoscopy acceptable
Rivaroxaban(once daily preparation)	CrCl >30mL/min	No rivaroxaban on day prior to and on day of procedure	No rivaroxaban for 2 days prior to and on day of procedure
	CrCl 15-30mL/min	No rivaroxaban for 2 days prior to and on day of procedure	No rivaroxaban for 3 days prior to and on day of procedure
Apixaban (twice daily preparation)	CrCl >30mL/min	No apixaban on day prior to and on day of procedure	No apixaban for 2 days prior to and on day of procedure
	CrCl 15-30mL/min	No apixaban for 2 days prior to and on day of procedure	No apixaban for 3 days prior to and on day of procedure
Dabigatran	CrCl >50mL/min	No dabigatran on day prior to and on day of procedure	No dabigatran for 2 days prior to and on day of procedure
	CrCl 30-50mL/min	No dabigatran for 2 days prior to and on day of procedure	No dabigatran for 4 days prior to and on day of procedure
Edoxaban	CrCl >50mL/min	No edoxaban on day prior to and on day of procedure	No edoxaban for 2 days prior to and on day of procedure
	CrCl 15-50mL/min	No edoxaban for 2 days prior to and on day of procedure	No edoxaban for 3 days prior to and on day of procedure

Creatinine clearance must be used for calculating renal function using the Cockroft and Gault equation (see below). eGFR is **not** a suitable alternative:
CrCl (ml/min)=(140 – age) x wt (kg) x 1.04 (female) or 1.23 (male) serum creatinine (micromol/l)
https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation

Restart
As soon as possible, provided the clinical situation allows and adequate haemostasis has been established as determined by the treating physician – usually within 2 to 3 days. **Endoscopist to specify on the endoscopy report.**
For patients at high risk of bleeding post-operatively where the initiation of the DOAC is delayed, consider prescribing a prophylactic dose of tinzaparin until adequate haemostasis has been established as determined by the responsible clinician. If required, seek haematology advice.

Perioperative Guidance for Antiplatelet management undergoing high risk therapeutic endoscopy procedures



Restart when risk of bleeding no longer significant (usually ~3- 4 days post procedure). Endoscopist to specify on the endoscopy report.

Aspirin

If prescribed, continue to take

Dipyridamole

Stop 24 hours prior to procedure

Restart when risk of bleeding no longer significant (usually ~3- 4 days post procedure).

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