PERIOPERATIVE MEDICATION GUIDELINES - ADULT

GUIDELINE

Most regular oral medications should be continued and may be administered up to when the patient leaves the ward to go to the operating theatre by giving with enough water to swallow the medication. The need for continued management of chronic conditions over-rides the issues of aspiration around oral dosing of medications. Uncontrolled hypertension, epilepsy, Parkinson's symptoms etc. cause serious management issues during surgery.

Alzheimer's medications Donepezil (Aricept®), galantamine (Reminyl®), rivastigmine (Exelon®)	**Recommendation: Continue**
These anticholinesterase inhibitors are likely to exaggerate succinylcholine-type relaxation during anaesthesia when given with suxamethonium and similar neuromuscular blocking agents. In general the use of suxamethonium will best be avoided.[2] If suxamethonium has to be given be aware that action might be prolonged.	

Angiotensin-Converting Enzyme Inhibitors	**Recommendation: generally withhold on the day of surgery**
Patients that have received angiotensin-converting enzyme inhibitors (ACE-I) until the morning of surgery, showed significantly more episodes of hypotension on induction of anaesthesia than those where the ACE-I had been stopped. [30,31] An increase in the incidence of hypertensive periods during the induction of anaesthesia was not seen. This is most likely due to the long half-life of the modern ACE-Is. Acute cessation of these drugs does not result in a critical reduction of drug concentration. These results are supported by a study that observed an increased incidence of post-intubation hypotensive episodes after a single dose of captopril.[46] In addition to their primary action ACE-I attenuate the metabolism of the potent vasodilator bradykinin. No study or case report has been published indicating harm from withholding ACE-I the day of surgery.	

Angiotensin II Receptor Antagonists[32]	**Recommendation: Generally withhold on the day of surgery**
The incidence and severity of hypotension during induction of anaesthesia was significantly higher in patients on AT receptor antagonists compared with patients receiving beta adrenoreceptor blockade, calcium channel blockers or ACE-Is. [33] Cessation of AT receptor antagonists on the morning of surgery resulted in a significantly reduced incidence of severe hypotension during induction of anaesthesia. [34] The need for vasoconstrictive intervention was significantly higher if AT receptor antagonists were given. Adequate treatment of these often quite severe hypotensive episodes could not be achieved by ephedrine or phenylephrine but required the administration of 1 mg boluses of a vasopressin system agonist (terlipressin). [33]	

Anticonvulsants	**Recommendation: Continue.**
Notes: Surgery type: Cessation of antiepileptic agents may be desirable before neurosurgery to excise the epileptic focus. In this case, benzodiazepines may be useful to prevent any peri-operative seizures as serum concentrations of anticonvulsants fall below the therapeutic threshold [60]. Pre-op review of such patients must include this information. Manage post-operatively via alternative routes if required.	

Antidepressants Tricyclic and SSRI only, see separate entry for MAOI's	**Recommendation: Continue** Cease 2 weeks before surgery if post-op bleeding is a major concern – see notes
Tricyclic antidepressants and selective serotonin (5HT) reuptake inhibitors affect neurotransmitter reuptake and receptor binding. Thus cardio-vascular effects of anaesthesia can be exaggerated[2,52]. Patients undergoing surgical procedures in which postoperative bleeding could lead to significant morbidity (such as CNS procedures) should have SSRI's discontinued several weeks prior to surgery[62] because of potential antiplatelet effects and the need to taper therapy in most cases. The decision to withhold SSRIs perioperatively should balance the consequences of bleeding with the severity of the psychologic disorder being treated. Patients with severe mood disorders should generally be maintained on SSRIs through surgery. Consultation with a psychiatrist is recommended to consider alternative therapies during the perioperative period for the rare patient with a severe mood disorder who is undergoing a procedure in which bleeding could lead to significant morbidity[62].	

Anti - Dyslipidaemic Agents HMG CoA-reductase inhibitors (statins), bile acid binding resins, fibrates, ezetimibe and nicotinic acid	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively.	

Antiemetics	**Recommendation: Continue**
Antiemetic requirements may change perioperatively. This will be determined by the anaesthetist	

Antihypertensives Except ACE-Inhibitors, Angiotensin-II-antagonists Beta-blockers and diuretics. See separate entries for these medications	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively.	

Analgesics	**Recommendation: Continue**
Analgesic requirements will likely increase peri-operatively. Withholding regular analgesics will exacerbate pain or even precipitate withdrawal symptoms.	

Antiarrhythmics including beta blockers	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively	

Antihistamines	**Recommendation: Withhold on day prior to and of surgery**
Due to the potential additive risk of sedation with general anaesthetics, the order should be withheld until postsurgical review. H2 antagonists should continue (see anti-reflux medications)	

Anti-reflux medications Antacids, H_2 antagonists, proton pump inhibitors	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively	

Antipsychotics/ anxiolytics /hypnotics/ benzodiazepines	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively, but patients on these agents should be brought to the attention of the anaesthetist in order to avoid peri-operative medication interactions.	

Aspirin	**Recommendation: Generally continue. Varies according to the indication and risk of perioperative bleeding**

Notes:

- Aspirin inhibits platelet aggregation by irreversibly inhibiting cyclo-oxygenase (COX), reducing synthesis of thromboxane A_2 (an inducer of platelet aggregation) for the life of the platelet.[1,2] Effect occurs rapidly (within 30 minutes) and lasts for the life of the platelet (8-10 days).[3,4,5] Aspirin increases bleeding times up to twice that of normal healthy subjects. However there is no evidence to suggest that bleeding time can predict haemostatic compromise.[6]
- Aspirin should only be discontinued perioperatively if aspirin's known or assumed perioperative bleeding risks and their sequelae are expected to be similar or more severe than the observed cardiovascular risks after aspirin withdrawal (MI, stroke, peripheral vascular occlusion or CV death)[58]
- In general, cease aspirin when risk of postoperative bleeding is high or when the consequences of even minor bleeding are significant, i.e. neurosurgery or retinal surgery, etc.[1,2,4,7,8]

In most cases where cessation is indicated, cease 7 days pre-operatively. If in doubt contact the anaesthetist, cardiologist or procedural specialist from appropriate area.

Asthma medications/COPD medications including inhaled medications	**Recommendation: Continue**
Inhalers can and should be used up to and immediately before surgery.	

Beta Blockers	**Recommendation: Continue**

- Randomised controlled trials on peri-surgical B blockers are lacking. Withdrawal of long-term beta-blocker therapy in several different patient populations has been associated with an elevation in heart rate, blood pressure and an increased risk of myocardial ischemia[59].
- Case reports of perioperative myocardial ischemia have also been documented in noncardiac surgical patients in whom propranolol hydrochloride was withdrawn[60].
- A 2008 randomised controlled trial was conducted in 8351 patients using extended-release metoprolol vs placebo for 30 days, starting 2-4 hours pre-op. Although metoprolol reduced the risk of myocardial infarction, cardiac revascularisation, and clinically significant atrial fibrillation 30 days after randomisation compared with placebo, the drug also resulted in a significant excess risk of death, stroke, and clinically significant hypotension and bradycardia[61].

Bisphosphonates alendronate, clodronate, etidronate, risedronate, tiludronate	**Recommendation: Cease from morning of surgery - see notes**

Notes:

Oral bisphosphonates are known to cause oesophageal ulceration. Administration guidelines[1] state that the patient should sit up for 30 mins after taking the dose, with a full glass of water. The drug should be withheld postoperatively until such time as the patient is able to do this.

Blood and blood forming agents Erythropoiesis Stimulating Agents e.g. epoetin	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively	

Calcium Channel Blockers	**Recommendation: Continue except nifedipine, see notes.**

- Long acting dihydropyridines have shown to be safe during surgery.27,28,29 Short acting dihydropyridines (nifedipine) cause sympathetic activation and should be avoided in patients at risk of myocardial ischemia. 28,29
- In patients at risk of myocardial ischemia taking nifedipine, consider changing nifedipine to another agent.

Clopidogrel (Plavix®, Iscover®)	**Recommendation: Varies according to indication, see notes**
Clopidogrel **irreversibly** inhibits platelet aggregation by inhibiting binding of adenosine diphosphate (ADP) to its specific platelet receptor, and the subsequent ADP-mediated activation of glycoprotein IIb/IIIa.[1,2,8] The antiplatelet effect is detectable at 2 hours, maximal between 3 and 7 days and persists for 4 to 8 days after cessation of therapy.[3] If surgery must be performed within 6 weeks of stent placement (or 1 year of placement of a drug-eluting stent) and the risk of major bleeding appears greater than the risk of stent thrombosis, clopidogrel should be discontinued for as brief a period as possible. To minimize perioperative bleeding, clopidogrel should be stopped at least five days before coronary artery bypass graft surgery. Some experts are willing to recommend shorter discontinuation periods, perhaps up to three days before cardiac or non-cardiac surgery, for procedures less likely to be associated with major bleeding. On the other hand, consideration may be given to discontinuing clopidogrel at least seven days before intracranial surgery, given the potentially disastrous consequences of intracranial bleeding. Clopidogrel should be restarted with a loading dose of 600 mg as soon as possible after surgery, perhaps even later in the day, if postoperative bleeding has stopped. Compared to 300 mg, this dose reduces the time to achieve maximal inhibition of platelet aggregation to two to four hours and, in the setting of recent surgery, minimizes the frequency of hypo-responsiveness to clopidogrel. **Summary: If being used for coronary artery stents or patients with TIA's then discuss stopping with prescribing cardiologist or neurologist; if in doubt contact the Anaesthetist, Cardiologist, or procedural specialist from appropriate area.** For other situations, cease 5 days pre-operatively[1,2,8,24.] .Consider substituting aspirin 100 mg/day if appropriate (as above).	

Contraceptives, Combined Oral	**Recommendation Varies according to type of surgery, see notes.**
Patients taking the Combined Oral Contraceptive (COC) and undergoing major surgery are at increased risk of post-operative venous thromboembolism[43] Altering contraceptive therapy may put the patient at risk of pregnancy which must be excluded prior to surgery.[43] **TYPE OF SURGERY** Patients undergoing elective major surgery or leg surgery should: [2,43] continue the COC and use thromboprophylaxis perioperatively (i.e. sc. low molecular weight heparin and graduated elastic compression stockings) **or:** stop the COC 4 weeks pre-operatively and use an alternative form of contraceptive e.g. barrier contraception	

COX-2 (cyclo-oxygenase-2) inhibitors celecoxib (Celebrex®), meloxicam (Mobic®)	**Recommendation: Continue**
Clinical trials with COX-2 inhibitors have shown no effect on platelet aggregation or bleeding times.[1,3,9]. However, all nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors can adversely affect renal function,[2] so this must be monitored in the postoperative period.	

Dermatological preparations Topical Corticosteroids	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively.	

Digoxin	**Recommendation: Continue**
Digoxin has a narrow therapeutic ratio, which is reduced by hypokalaemia. Dysrhythmias caused by digitalis toxicity can present as ventricular arrhythmias, nodal tachy- or bradycardia, sinoatrial block, AV-block of various degrees of severity and ventricular tachycardia. Withholding digoxin the morning of surgery will reduce the chance of toxicity[35] but attenuate the cardiac stability provided in adequately treated patients. [36,48]	

Diuretics	**Recommendation: Consider withholding on morning of surgery**
With little evidence available most experts recommend stopping diuretic therapy on the day of surgery. Rationale: • avoid further volume loss in volume depleted patients • reduce the possibility of resultant hypokalaemia, hypocalcaemia and hypomagnesaemia.	

Dipyridamole	**Recommendation: Continue unless combined with aspirin, see notes**
Notes: Cessation of dipyridamole is not required in most cases, since the drug does not affect bleeding time[57]. Note, however, if combined with aspirin, management should be guided by the aspirin component, as detailed under aspirin section.	

Genitourinary drugs Anticholinergics, desmopressin, alpha blockers, finasteride	**Recommendation: Continue**
There is some evidence that certain alpha blockers should be withheld prior to cataract surgery due to concerns with 'floppy iris syndrome'. Patients falling into such categories must have appropriate pre-op review.	

Glaucoma preparations – Ocular topical	**Recommendation: Continue unless patient is having ophthalmological surgery**
There is no evidence that these medications should be withheld perioperatively.	

Herbal/Natural Supplements Natural therapies are often a mixture of preparations, not always in highly purified form, which may exhibit unusual and poor bioavailability.[2] In addition, preparations may be contaminated by other	**Recommendation: As it is difficult to assess the potency of constituents contained in natural products, it is recommended that all natural therapies be ceased at least one-week pre-operatively.[2,8,10,11,12,13]**

Herbal/Natural Supplements known to affect bleeding time or interact with anaesthetics/other medications:[10-13]		
Alfalfa	Fenugreek	Meadowsweet
Aloe	Feverfew	Omega 3 Fish Oils
Angelica	Fucus	Papaya/Papain
Aniseed (Anise)	Garlic	Peppermint
Arnica	Ginger	Poplar
Asafoetida	Ginkgo biloba	Prickly Ash (North and South)
Belladonna	Ginseng	Pulsatilla
Black cohosh (Remifemin®)	Goldenseal	Quassia
Celery	Grapeseed	Red Clover
Chamomile (German and Roman)	Horse-chestnut	Saw Palmetto
Clove oil (eugenol)	Horseradish	St John's Wort
Danshen	Kava Kava	Trifolium
Dietary Supplements	Kombucha Tea	Valerian
Dong Quai	Liquorice	Vitamin E
Echinacea	Lobelia	Willow
Evening Primrose Oil	Ma Huang (Ephedra)	Yohimbine

HIV agents	**Recommendation: Continue**
Notes: Because resistance to these medications develops so easily, patients should not miss doses and should maintain an "all or none" approach to taking them. In the peri-operative period these medications should be continued up to the time of surgery, stopped together, and then restarted together when the patient can tolerate oral medication. No significant drug reactions have been reported between antiretrovirals and anaesthetic agents[2]	

Hormone Replacement Therapy (HRT) and hormone antagonists: oestrogens, raloxifene, tamoxifen, tibolone	**Recommendation: Varies according to surgery type, see notes.**

Notes:

Patients taking Hormone Replacement Therapy (HRT) and undergoing major surgery, are at increased risk of post-operative venous thromboembolism.[43,44,45]

40 per cent of VTE's in women taking tamoxifen occur within 3 months of surgery or immobility. However a decision to cease it perioperatively several weeks before surgery must be discussed with the oncologist.

Surgery Type

Patients undergoing elective major surgery or leg surgery should: [43,44,45]

continue HRT and use thromboprophylactic measures in the peri-operative period (i.e. sc. low molecular weight heparin and graduated elastic compression stockings)

or

cease these agents 4-6 weeks prior to surgery. This option is advisable if the patient has predisposing risk factors for VTE: personal history of VTE, family history of VTE in a first degree relative under 45, obesity, trauma, long term immobilisation or varicose veins[60].

Immunosuppressants *Calcineurin inhibitors*: cyclosporin, tacrolimus *Antimetabolites*: mycophenolate, azathioprine *MTOR inhibitors*: sirolimus, everolimus	**Recommendation: Varies with drug and surgery type, see notes**

Calcineurin inhibitors: There is no evidence that these medications should be withheld perioperatively. Furthermore, brief discontinuation can result in rejection of transplanted tissues or organs.

MTOR inhibitors should be avoided perioperatively due to high incidence of impaired wound healing.

Overall summary: Review by prescribing specialist one month prior to surgery date.

Insulin	**Recommendation: See Guidelines for Adult Diabetics Treated with Insulin**

Diabetic control should be optimised prior to surgery as peri-operative management is easier when the patient has good peri-operative metabolic control.[14,15,16]

Laxatives Stimulant, Osmotic, stool softeners and bulk forming	**Recommendation: Withhold on the morning of surgery**

Laxative requirements may change perioperatively due to reduced oral intake or opioid initiation. MO to review postoperatively.

Lithium	**Recommendation: Cease at timeframe according to surgery type, see notes.**

Notes:

The therapeutic index of lithium is quite narrow; toxicity (> 1.2 mmol/L) may manifest with nausea, and vomiting. Higher concentrations may cause sedation, muscle weakness, hypotension, wide QRS complex, cardiac dysrhythmias, delirium, seizures and coma. [38,39]

Lithium impairs renal concentrating ability by inhibition of renal tubular adenosine monophosphate formation. This will cause polyuria and possibly hypovolaemia in about 20% of patients chronically treated with lithium. In the presence of lithium the effects of non-depolarising neuromuscular blocking agents might be prolonged.

Surgery Type

Lithium should be withheld 24 hours before minor surgery and 2 days prior to major surgical procedures. [7,36,40]

Lithium should be restarted soon after surgery. [7,49] when renal function and fluid & electrolyte balance (especially any hyponatraemia) return to normal[60]

Lithium serum concentration should be monitored before elective surgery.

Metformin Diabex®, Diaformin®, Glucohexal®, Glucomet®, Glucophage®	**Recommendation: Withhold the night before and the day of Surgery. See Guidelines for Adult Diabetics Treated with Oral Hypoglycaemics**

Notes:

Metformin has been associated with the development of lactic acidosis, which, although rare, can be fatal.[17,18,19]

Replace with insulin infusion if necessary. Restart after 2-3 days when it is certain that no acute renal dysfunction has developed peri-operatively.[1,2]

Methotrexate	Recommendation: Withhold 48 hours before surgery

Notes:
During the perioperative period, fluid restriction can lead to hypovolaemia and diminished renal function. Methotrexate is predominantly cleared from the body by the kidneys so it is prudent to withhold it 48 hours before surgery or any other procedure associated with even transient renal insufficiency[60]. Methotrexate toxicity can also be enhanced by certain general anaesthetics e.g. Nitrous Oxide[1]

Monoamine Oxidase Inhibitors (MAOIs)	Recommendation: Continue but check with anaesthetist

Notes:
Patients on irreversible MAOIs (e.g. phenelzine (Nardil®) and tranylcypromine (Parnate®)) should be brought to the attention of the anaesthetist in order to avoid peri-operative medication interactions. DO NOT USE pethidine for post-operative pain relief; use other opioids with caution and at a reduced dose.[20,21,22]
Patients on moclobemide can have their medication withheld on the morning of surgery, should the use of pethidine be necessary.
The administration of opioids, most commonly pethidine, to patients on MAOI's may result in an excitatory or depressive reaction that is characterised either by agitation, headaches, hyperpyrexia, muscle rigidity, seizures and coma or by hypotension, respiratory depression and coma respectively.
Recent expert opinion recommends continuation of MAOIs to avoid the risk of disease exacerbation after discontinuation of effective therapy.[62]
Combinations of MAOIs and pethidine MUST be avoided.

Non-Selective Nonsteroidal Anti- Inflammatory Drugs (NSAIDs)	Recommendation: Consider ceasing 3 days pre-operatively[1,2,5,7]

Notes:
- NSAIDs inhibit cyclo-oxygenase which reduces thromboxane A_2 production and release resulting in reduced platelet aggregation and increased bleeding time.[6] NSAIDs **reversibly** inhibit platelets.[2,5]
- NSAIDs can also adversely affect renal function.[1,2] This effect may be accentuated if dehydration or renal hypoperfusion exist (since reduced renal blood flow increases the importance of intrarenal prostaglandins in maintaining renal function).[1]

Exceptions to the 3 day rule:
- Ibuprofen and indomethacin[1,2] have shorter half-lives (2-5 hours) and can be stopped 1 day before surgery. Diclofenac, diflunisal and sulindac can also be stopped 1 day prior to surgery [56].

Oral Hypoglycaemics (see metformin above) i.e: acarbose, glibenclamide, gliclazide glimepiride, glipizide pioglitazone, rosiglitazone (not in combination), repaglinide	Recommendation: Cease day of surgery only See Guidelines for Adult Diabetics Treated with Oral Hypoglycaemics

Notes[57]:
Preoperative management:
- Omit Metformin night before and day of procedure
- Omit all other oral hypoglycaemics on morning of surgery only
- Check BSL on arrival and 2 hourly thereafter
- If BSL < 5 mmol/L
  - Contact procedural anaesthetist (or equivalent)
  - Start IV Fluids (5% Glucose at 100 mL/h)
- If BSL > 10 mmol/L
  - Contact procedural anaesthetist (or equivalent)
  - Consider insulin infusion*

Postoperative management:
- BSL should be measured and recorded immediately after procedure, at 2 hrs, 4 hrs, and then 4 hourly while in hospital.
- Notify Procedural Anaesthetist or RMO if BSL < 5 or > 10 mmol/L
- Patient should return to usual treatment (except metformin - see above) when consuming oral fluids and food
- Major Surgery: During early post-surgical phase, physiological stress may increase insulin requirements. The patient may need an insulin infusion to maintain euglycaemia. See separate guideline on Insulin infusion.

Parkinson's disease medication	**Recommendation[1]: Continue**
Notes: The withdrawal of levodopa therapy may cause an exacerbation of symptoms and a neuroleptic malignant syndrome. Even brief interruptions of antiparkinson medication during surgery may produce increased muscle rigidity. Levodopa should be given in the morning of surgery and should be continued. Manage post-operatively via alternative routes. A case report even suggested the enteral administration of levodopa for long surgical procedures; thus avoiding the side effects of an intravenous dose. [42]	

Proton pump inhibitors and H2 antagonists	**Recommendation: Continue**
There is no evidence that these medications should be withheld perioperatively	

Corticosteroids including inhaled medications	**Recommendation[37]: Continue**
Notes: Patients on long term oral corticosteroids (> 3 months) may have adrenal suppression and require higher doses pre-operatively or hydrocortisone IV preoperatively.	

Ticlopidine	**Recommendation: Determined by indication, see notes**
Notes: Ticlopidine is an irreversible inhibitor of platelet aggregation with a similar mechanism of action to clopidogrel.[1,3] When taken orally, bleeding time is prolonged two to five times baselines values.[19] The effect is irreversible.[1] Thienopyridine derivatives demonstrate both time- and dose-dependent effects; with steady state after 7 days for clopidogrel and 14-21 days for ticlopidine.[25] **Indication:** Particularly complex in patients with coronary artery stents. In most cases cease 10-14 days pre-operatively, but this will be determined by the indication for ticlopidine – seek specialist advice from surgeon, anaesthetist, or specialist from appropriate area.[2,8,24]	

Thyroxine	**Recommendation: Continue**
There is no evidence that this medication should be withheld perioperatively	

Topical anti-infectives and anti-inflammatories Antibiotic eye drops, corticosteroid eye drops, other drops for allergic eye conditions, creams.	**Recommendation: Continue except in the case of ocular surgery.**
There is no evidence that these medications should be withheld perioperatively. The absorption of drug from topical application of NSAIDS is reported to be minimal. No case reports have been found citing perioperative complications resulting from the use of these agents[57].	

Vitamin and electrolyte preparations Multivitamins, vitamin b12, folic Acid, pyridoxine, calcitriol, oral iron preparations, oral potassium supplements, phosphate binders	**Recommendation: Continue, except potassium preparations.**
There is no evidence that these medications should be withheld perioperatively. Potassium supplements should be withheld due to the danger of hyperkalaemia, at the discretion of the anaesthetist.	

Warfarin	**Recommendation: generally ceased 4-5 days prior to surgery. Varies according to indication for Warfarin - Refer to Guidelines for Warfarin Therapy & Planned Procedures**
Notes: Warfarin inhibits the synthesis of vitamin K dependent coagulation factors.[1] This results in depression of factors II, VII, IX and X and prolongation of bleeding time.[1] The effect on coagulation lasts from 20-60 hours, with a mean of about 40 hours.[24] Perioperative management of warfarin depends on the patient's risk status for thromboembolism and surgery type. Ensure adequate anticoagulation cover if high risk. **Note that low risk superficial procedures may not require cessation of anticoagulation. Consultation with anaesthetist is advised.**	

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Parts of this document have been adapted from guidelines published by Queensland Health; the Department of Anaesthesia and Critical Care Medicine, University Hospital of Muenster, Germany; NMSBC Pre-Admission Clinic Project team – The Canberra Hospital; and the Division of Pharmacy, Flinders Medical Centre.

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