Drug Prescribing Guideline

Health
Hunter New England
Local Health District

Document number: JHH_BH_0077

Perioperative management of medications

Sites where Local Guideline applies	John Hunter Hospital and Belmont Hospital
Target audience	Clinical staff involved in the care of perioperative patients
This Local Guideline applies to:	
1. Adults	Yes
2. Children up to 16 years	No
3. Neonates – less than 29 days	No
Description	This guideline provides general advice about the management of medications in the perioperative period
Keywords	Perioperative, medications, anaesthesia, surgery

Go to Guideline

Replaces existing document?	Yes
Registration number and dates of superseded documents	JHH_JHCH_BH_0257

Relevant or related Documents, Australian Standards, Guidelines etc:

- NSW Health Policy Directive PD2012_069 Health Care Records – Documentation and Management
- NSW Health Policy Directive PD2022_032 Medication Handling
- NSW Health Policy Directive PD2012_069 Care Coordination: Planning from Admission to Transfer of Care in NSW Public Hospitals
- NSW Health Policy PD2019_020:PCP 7 and PD2021_033:PCP 2 Patient Identification Procedures

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Prerequisites (if required)	This document refers to both prescribed and over the counter medications, and is relevant to patients having elective and emergency procedures
Local Guideline note	This document reflects what is currently regarded as safe and appropriate practice. This guideline does not replace the need for the application of clinical judgment in respect to each individual patient. If staff believe that the guideline should not apply in a particular clinical situation they must seek advice from their unit manager/delegate and document the variance in the patient's health record. If this document needs to be utilised outside of the John Hunter Hospital please liaise with the local Perioperative and Pharmacy Services to ensure the appropriateness of the information contained within the Guideline and Procedure.

Date initial authorisation:	14th March 2024
Authorised by:	Quality Use of Medicines
This document contains advice on therapeutics	Yes Approval gained from Local Quality Use of Medicines Committee on 14/3/2024
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Position responsible for review:	Director of Perioperative Services
Date Reviewed:	March 2024
Review due date:	March 2026
Version:	1.0 19th April 2024

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PURPOSE AND RISKS

Many patients undergoing surgery will be taking medications on a regular basis. Clinical staff involved in the care of these patients must decide if chronic medications should be continued in the perioperative period. Inappropriate continuation or cessation of chronic medications can result in poor clinical outcomes. Clear and consistent medication advice allows patients and staff to minimise the risk of medication errors that may adversely affect patient care.

This document aims to provide general advice about common medications, medications with known perioperative effects and those known to interact with anaesthetic agents. The decision to continue or withhold medications will be influenced by individual patient factors, along with the type of procedure being performed. Where there is uncertainty, perioperative management of chronic medications should be discussed with the anaesthetist, surgeon or specialist responsible for the patient's care.

Risk Category*:* Clinical Care & Patient Safety

GLOSSARY

Acronym or Term	Definition
CrCl	Creatinine Clearance, surrogate marker for renal function
DOAC/NOAC	Direct oral anticoagulant/Novel oral anticoagulant
GLP-1	Glucagon-like peptide 1
HRT	Hormone replacement therapy
MAOI	Monoamine oxidase inhibitor
NMBDs	Neuromuscular blocking drugs
NDNMBDs	Non-depolarising neuromuscular blocking drugs
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NSAID	Non-steroidal anti-inflammatory drug
RFA	Request for admission
SERM	Selective estrogen receptor modulator
SGLT	Sodium-glucose co-transporters

SLE	Systemic lupus erythematosus
SNRI	Serotonin and noradrenaline reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
TCA	Tricyclic antidepressant
VTE	Venous thromboembolism

John Hunter Hospital / Service Manager Responsibility

- Ensure that the principles and requirements of this procedure are applied, achieved and sustained
- Ensure effective response to, and investigation, of alleged breaches of this procedure.
- Ensure all staff have completed My Health Learning online module Introduction to Safety and Quality (course number 42189807)
- Notify staff of all new and revised local procedures and guidelines through the JHH Newsletter

Line management responsibility

- Notify staff of new and revised policies, procedures and guidelines relevant to the workplace / unit / clinical specialty.
- Post the JHH newsletter (with policy, procedure and guideline updates) in staff rooms
- Identify high clinical risks relevant to patient population of unit/specialty and undertake audits of compliance with relevant policies, procedures or guidelines.

Employee responsibility

Staff must:

- Comply with policies, procedures and guidelines applying to their workplace / unit / specialty
- Report unsafe practices, equipment or environment to line manager
- Escalate any patient safety concerns to line manager, including if it is assessed that policies, procedures or guidelines do not reflect contemporary practice
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GUIDELINE

This Guideline does not replace the need for the application of clinical judgment in respect to each individual patient.

Most regular oral medication should be continued on the day of surgery, and can be administered with a sip of water (< 50mL) until the time of surgery.

<u>General Principles of Perioperative Medication Management</u>

- A complete medication history should be obtained for every patient requiring a general anaesthetic or procedural sedation. This should include all prescription, over-the-counter and herbal or complementary medications. Care should be taken to enquire specifically about inhaled or injected medications, as these may be missed. In addition, information relating to substance use (e.g. nicotine, alcohol, and illicit drugs) should be sought.
- For medications where abrupt cessation may result in withdrawal symptoms, consider continuing or tapering medications if appropriate and feasible.
- Consider the potentially altered metabolism and elimination of medications during the perioperative period, as well as the potentially impaired gastrointestinal absorption of oral medications.

- Consider alternative routes for important oral medications where the oral route is likely to be unavailable for a prolonged period in the perioperative setting.
  Condensed medication advice

Table 1 summarises the instructions regarding common or important medications that are encountered in patients perioperatively.
For more detailed notes, and a comprehensive list of medications, see **Table 2.**

Table 1. Common or important medications that may need to be ceased or reduced in the perioperative period

Class	Continue/Omit
ACE inhibitors ("prils") or Angiotensin receptor inhibitors/blockers (ARBs) ("sartans")	Omit day of surgery
Analgesics	Continue paracetamol and opioids. See Table 2. below for NSAIDs.
Anticoagulants	Discuss with proceduralist. If withholding, discontinue for the following duration: - heparin: 6 hrs - enoxaparin: 24 hrs for therapeutic dosing, 12 hrs for prophylactic dosing (longer delays are required for patients with CrCl < 30 mL/min) - warfarin: 5 days, consider need for bridging therapy - DOACs/NOACs: 72 hours (dabigatran: withhold for 96hrs if CrCl 30-50 mL/min)
Antiplatelets	Discuss with proceduralist. If withholding, discontinue for the following duration: - aspirin: 5 days - clopidogrel: 7 days - prasugrel: 7 days - ticagrelor: 5 days - ticlopidine: 14 days For antiplatelet agents refer to Guideline "Perioperative management of antiplatelet agents"
Anticonvulsants	Continue
Antidepressants, including monoamine oxidase inhibitors (MAOIs)	Continue If continued, ensure procedural anaesthetist is aware (e.g. via a warning note). A MAOI-safe anaesthetic technique should be used (see detailed notes below). Avoid the use of other serotonergic drugs during the perioperative period.
Anti-Parkinson's medications	Continue Refer to Guideline "Perioperative Management of Patients with Parkinson's Disease"
Beta blockers and antiarrhythmics	Continue
Bisphosphonates	Omit day of surgery
Corticosteroids	Continue Consider need for steroid supplementation perioperatively (see detailed notes below)
Diuretics (loop and potassium-sparing)	Omit day of surgery, unless indicated for heart failure/fluid overload

Herbal products	Omit 7 days prior to surgery
Hormone Replacement Therapy	Continue. Consider ceasing 4-6 weeks prior to surgery if high risk of VTE e.g. prolonged immobilisation
Insulin	**Day of surgery:** Ultra and short-acting: omit day of surgery Pre-mix: half of normal dose Long-acting: normal dose or reduce to 80% of normal dose if hypoglycaemia of concern **Day before surgery:** Normal dose for all Refer to Guideline "Glycaemic management in patients awaiting elective surgery"
GLP-1 analogues	Recommend stopping one week prior to surgery where able. Consider withholding for > 1 week if there is a high risk of post-operative nausea, vomiting and/or ileus.
Lithium	Minor surgery: continue Major surgery: withhold 24hrs prior to day of surgery
Oral contraceptive pill	Low-moderate thromboembolism risk: continue High thromboembolism risk: omit day of surgery and restart when mobile
Oral hypoglycaemic agents (anti-diabetic medication)	Omit day of surgery SGLT-2 inhibitor: **omit 3 days prior** to day of surgery. Monitor ketones and reintroduce cautiously, once eating and drinking normally. Refer to Guideline "Glycaemic management in patients awaiting elective surgery"

Detailed medication advice

The following table provides detailed medication advice. This list is not exhaustive. Where a medication is not included below, please discuss with the anaesthetist, proceduralist, or prescriber.

Table 2. Detailed medication advice

Central Nervous System (CNS)			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Anticonvulsants	Carbamazepine, gabapentin, lamotrigine, levetiracetam, phenytoin, pregabalin, topiramate, valproate	Continue	Consider phenytoin level if recent dose adjustment without subsequent serum level, or concerns regarding compliance or toxicity (1)
Anti-Parkinsonian medications	*Dopamine agonists:* apomorphine, bromocriptine, cabergoline, pramipexole, rotigotine *Dopamine precursors:* levodopa-benserazide, levodopa-carbidopa *Monoamine oxidase B inhibitors:* rasagiline, safinamide, selegiline *Catechol-O-methyltransferase inhibitors (COMTIs):* entacapone	Continue	If a prolonged period of NBM is anticipated post-operatively, discuss with neurologist and consider converting to a rotigotine patch preoperatively. Abrupt withdrawal of treatment may cause an exacerbation of symptoms, and may result in symptoms which resemble neuroleptic malignant syndrome. Refer to Guideline "Perioperative Management of Patients with Parkinson's Disease" (2)
Antipsychotics	*Typical:* chlorpromazine, haloperidol *Atypical:* clozapine*, olanzapine, quetiapine, risperidone	Continue	Both typical and atypical antipsychotics may prolong the QT interval and cause arrhythmia. Discuss with psychiatrist in patients whose ECG demonstrates prolongation of QT interval (2). *Refer to Guideline "Perioperative Management of Patients Taking Clozapine"
Benzodiazepines	Alprazolam, bromazepam, clobazam, clonazepam, diazepam, flunitrazepam, lorazepam, nitrazepam, oxazepam, temazepam	Continue	Abrupt discontinuation can lead to withdrawal symptoms including hypertension, agitation, delirium and seizures. (2)

Anticholinesterases in Alzheimer's disease	Donepezil (Aricept), galantamine, rivastigmine	Continue	Be aware of drug interactions with NMBDs: - may antagonise the effects of NDNMBDs - larger doses may be needed - neostigmine may be ineffective as a reversal agent - expected to prolong the effect of suxamethonium (3,4)
Lithium		Continue for minor surgery Cease 24 hrs prior for major surgery	Check levels if not done in preceding 6 months Careful attention to fluid and electrolyte monitoring perioperatively. Consider thyroid function tests and ECG prior to surgery if not done recently. Be aware of drug interactions: - may reduce anaesthetic requirements - potentially prolongs effects of NMBDs (appropriate neuromuscular monitoring should be used) - NSAIDs increase lithium levels, avoid use. - risk of developing serotonin syndrome with opioids, ondansetron, methylene blue (2,5,6).
Tricyclic antidepressants	Amitriptyline, clomipramine, dosulepin/dothiepin, doxepin, imipramine, nortriptyline	Continue	Avoid the use of other serotonergic drugs during the perioperative period (See Appendix A) (2)
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline	Continue	Avoid the use of other serotonergic drugs during the perioperative period (See Appendix A) (2)
Serotonin and noradrenaline reuptake inhibitors (SNRIs)	Desvenlafaxine, duloxetine, venlafaxine	Continue	Avoid the use of other serotonergic drugs during the perioperative period (See Appendix A) (2)
Monoamine oxidase inhibitors (MAOIs)	*Reversible:* moclobemide *Non reversible:* phenelzine, tranylcypromine	Discuss with anaesthetist and psychiatrist. Warning note required: Risk of serotonin syndrome and/or hypertensive crisis in perioperative period	If continued, a MAOI-safe anaesthetic technique should be used, avoid: - cocaine, - indirect-acting sympathomimetics (eg. ephedrine, metaraminol), - ketamine - pethidine and - suxamethonium Consider premedication with benzodiazepines to reduce stress which may lead to sympathetic stimulation (2)

Other antidepressants	Agomelatine, mianserin, mirtazapine, reboxetine, vortioxetine	Continue	
Psychostimulants (used for treatment of attention deficit hyperactivity disorder)	Lisdexamfetamine (Vyvanse), dexamfetamine, methylphenidate* (Concerta, Ritalin)	Withhold day of surgery	May increase risk for hypertension and arrhythmias, lower the seizure threshold, and interact with medications that could be needed in the perioperative period (eg. vasopressors). *There is a risk of sudden blood pressure increase when halogenated anesthetics are used in conjunction with methylphenidate (2)
Substance misuse medications	Acamprosate, disulfiram*, naltrexone, buprenorphine (Subutex, Buvidal/Sublocade), buprenorphine/naloxone (Suboxone), varenicline, methadone	Continue Naltrexone: **Specialist advice required.** Discuss with prescribing drug and alcohol physician. If recommend to discontinue prior to surgery: - oral naltrexone: 3 days - extended release naltrexone: one month	*Disulfiram-alcohol reaction can be precipitated by exposure to ethanol/alcohol, even in small quantities found in topical preparations. Check excipients of any products used. Disulfiram inhibits the metabolism of some benzodiazepines (eg. diazepam) causing increased plasma concentration and therefore increased sedation. Methadone may prolong QT interval. Inform anaesthetist if patient is using naltrexone. Maximize non-opioid methods for perioperative pain control, including ketamine and regional anesthesia if possible. If opioids are required while naltrexone is still in effect (ie. within three days of oral naltrexone or within one month of extended-release naltrexone), opioids should be titrated to effect with close monitoring (1,7).
Cardiovascular			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Angiotensin Converting Enzyme (ACE) inhibitors	Captopril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolapril	Omit morning of surgery	Consider continuing in patients with difficult to control blood pressure and/or procedures with minimal anticipated fluid shifts (2)
Angiotensin Receptor Inhibitors/Blockers (ARBs)	Candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan	Omit morning of surgery	Consider continuing in patients with difficult to control blood pressure and/or procedures with minimal anticipated fluid shifts (2)
Angiotensin Receptor Neprilysin Inhibitors (ARNIs)	Sacubitril (available as Entresto - sacubitril + valsartan)	Omit morning of surgery	Consider continuing if prescribed for severe heart failure with reduced ejection fraction. (8,9)

Alpha blockers	Prazosin, tamsulosin, alfuzosin, silodosin	Continue	Inform surgeon if patient booked for eye surgery - risk of Intraoperative Floppy Iris Syndrome (IFIS) (1)
Anti-anginals	*Nitrates:* glyceryl trinitrate (patches and sublingual formulations), isosorbide dinitrate, isosorbide mononitrate *Other:* ivabradine, nicorandil, perhexiline*	Continue	*Consider obtaining a perhexiline level if not done within 3 months (1)
Anti-arrhythmics	Amiodarone, digoxin, disopyramide, flecainide, sotalol, verapamil, mexiletine, dofetilide	Continue	(8)
Anticoagulants	Heparin, enoxaparin, warfarin	Consider indication for use, surgical bleeding risk, and potential for neuraxial technique.	Discuss with proceduralist, anaesthetist, haematologist, or prescriber where indicated. If withholding, discontinue for the following duration: - heparin: 6 hrs - enoxaparin: 24 hrs for therapeutic dosing, 12 hrs for prophylactic dosing (longer delays are required for patients with CrCl <30 mL/min) - warfarin: 5 days, consider need for bridging therapy Refer to CEC Guidelines on Perioperative Management of Anticoagulant and Antiplatelet Agents (10)
	Direct oral anticoagulants (DOACs): apixaban, rivaroxaban dabigatran*	Withhold for 72 hrs (or as per RFA). If withheld for a shorter time, need to consider: • Renal function • Bleeding risk • Neuraxial anaesthesia • surgical preference	*For patients taking dabigatran with CrCl 30-50 mL/min, withhold for 96 hrs (4 days) Refer to CEC Guidelines on Perioperative Management of Anticoagulant and Antiplatelet Agents (10)

Antiplatelets	Aspirin, clopidogrel, prasugrel, ticagrelor	Refer to Guideline 'Perioperative management of antiplatelet agents'	Refer to "Perioperative management of antiplatelet agents" Guideline Multidisciplinary advice (cardiology, neurology, haematology) may be required in complex cases. Consider indication for use and surgical bleeding risk. Generally, discontinue for the following duration: - aspirin: 5 days - clopidogrel: 7 days - prasugrel: 7 days - ticagrelor: 5 days - ticlopidine: 14 days Or as per proceduralist or RFA instructions.
Beta blockers	Atenolol, carvedilol, metoprolol, propranolol, bisoprolol	Continue	(8)
Calcium antagonists	Diltiazem, verapamil, amlodipine, nifedipine	Continue	(2)
Diuretics - loop and thiazide	Bumetanide, chlorthalidone, furosemide, hydrochlorothiazide, indapamide, metolazone	Consider continuing for patients with heart failure in whom fluid balance has been more difficult to control	(2)
Diuretics - potassium-sparing	Amiloride, eplerenone, spironolactone	Consider continuing for patients with heart failure in whom fluid balance has been more difficult to control	(2)
Phosphodiesterase 5 inhibitors	Sildenafil, tadalafil	Cease 24 hours before surgery if taking PRN for erectile dysfunction Continue if prescribed and used regularly for pulmonary hypertension	(8)
Other antihypertensives	Clonidine, diazoxide, hydralazine, methyldopa, minoxidil, moxonidine	Continue	(2)
Statins	Atorvastatin, fluvastatin, pravastatin, rosuvastatin, simvastatin	Continue	(2)

Non-statin lipid lowering agents	Colestyramine, ezetimibe, fenofibrate, gemfibrozil, nicotinic acid	Cease day prior to surgery	Niacin and fibric acid derivatives (gemfibrozil, fenofibrate) cause myopathy and rhabdomyolysis. The risk is higher when these agents are used in combination with statins, and surgery may also increase the risk of myopathy. Lipid-lowering agents that are bile sequestrants (cholestyramine and colestipol) interfere with bowel absorption of multiple medications that may be required perioperatively (2).
Endocrine			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Anti-obesity medication	Phentermine (Duromine), diethylpropion (Amfepramone)	Cease 7 days prior to surgery	(11,12)
Antiresorptive therapy	Denosumab (Prolia)	Continue*	*Patients undergoing major orthopaedic surgery (joint replacement, revision, and spinal surgery) and procedures involving the jaw, inform surgeon and **ensure last dose is given more than 12 weeks' preoperatively.** (1)
	Bisphosphonates (alendronate, ibandronic acid, risedronate)	Omit morning of surgery	Risk of oesophageal ulceration. Recommence when patient able to sit upright for 30 minutes post dose (2)
Insulin	*Long-acting:* Glargine - Toujeo, Optisulin Determir - Levemir *Premixed long-acting:* Ryzodeg 70/30 *Pre-mixed*: Humalog Mix25 Humalog Mix50, NovoMix 30, Mixtard 30/70, Mixtard 50/50, Humulin 30/70 *Intermediate-acting*: Isophane - Protophane, Humulin NPH *Short-acting and ultra-short acting:* Neutral – Actrapid, Humulin R Aspart	See Guideline 'Glycaemic management in patients awaiting elective surgery' Day before procedure: normal dose for all Day of surgery: *Long-acting:* normal dose, reduce to 80% of normal dose if hypoglycaemia of concern. *Pre-mixed and intermediate insulin:* half of normal dose *Short-acting and ultra-short acting insulin:* omit	Refer to Guideline "Glycaemic management in patients awaiting elective surgery"

	– NovoRapid, Fiasp, Lispro – Humalog, Glulisine – Apidra		
Oral hypoglycaemic agents	*Biguanides:* metformin *Sulphonylureas:* glibenclamide, gliclazide, glimepiride, glipizide *DPP-IV inhibitors:* alogliptin, linagliptin, sitagliptin, saxagliptin, vidagliptin *Thiazolidinediones:* pioglitazone *Alpha-glucosidase inhibitors:* acarbose *SGLT2 inhibitors* (aka "-flozins"): dapagliflozin, empagliflozin, ertugliflozin	Cease SGLT2 inhibitors 3 days preoperatively Withhold other oral hypoglycaemic agents on day of surgery	Refer to Guideline "Glycaemic management in patients awaiting elective surgery". Do not restart SGLT2 inhibitors until patient eating and drinking normally.
Non-insulin injectable agents	*GLP-1 analogues (daily dosing):* exenatide (Byetta), liraglutide (Victoza, Saxenda) *GLP-1 analogues, weekly dosing*:* dulaglutide (Trulicity), semaglutide (Ozempic) *GIP and GLP1 analogue*:* Tirzepatide (Mounjaro)	Continue as normal *Recommend stopping one week prior to surgery where able. Consider withholding for > 1 week if there is a high risk of post-operative nausea, vomiting and/or ileus.	Refer to Guideline "Glycaemic management in patients awaiting elective surgery" Case reports of aspiration with long-acting GLP-1 analogues have occurred, even when patients are appropriately fasted. Long half-life of weekly GLP-analogues may limit the utility of withholding for 1 week, however withholding for > 2 weeks may worsen glycaemic control and require gradual reintroduction post-operatively. Consider full stomach precautions in patients on long acting GLP1-analogues
Corticosteroids		Continue	Consider need for stress dosing if taking > 5mg prednisolone daily for ≥ 3 weeks (13,14)

Combined oral contraceptives	Ethinylestradiol or estradiol in combination with a progrestogen (drospirenone, levonogestrol, nomegestrol, desogestrel, norithesterone)	Continue*	Oestrogen containing preparations increase the risk of postoperative VTE. *Consider ceasing 4-6 weeks prior if prolonged immobilisation expected after surgery. Potential interaction with perioperative agents (eg. sugammadex). Counsel patient for missed pill advice: Family Planning Australia - Missed COC pill advice (2)
Progesterone only contraceptives	Dienogest, drospirenone, etonogestrel, levonorgestrel, medroxyprogesterone, norethisterone, progesterone	Continue	Potential interaction with perioperative agents: counsel patient to follow the instructions for missed pill for oral agents, and to use non-hormonal contraceptive methods for 7 days for non-oral progesterone agents (eg. Implanon, hormonal intrauterine devices) (2)
Selective Oestrogen Receptor Modulators (SERMs)	Raloxifene, tamoxifen, toremifene	Continue*	These medications contain oestrogen or have pro-oestrogenic effects. *For surgery with a high-risk of VTE consider discontinuing based on specific SERM and indication for use (2). Cessation should only be done in conjunction with prescriber/oncologist.
Hormone Replacement Therapy (HRT)	Bazedoxifene with conjugated estrogens, conjugated estrogens, estradiol, estriol, tibolone	Continue*	Oestrogen containing preparations increase the risk of postoperative VTE. This should be taken into consideration when calculating VTE risk and considering VTE prophylaxis. *Consider ceasing 4-6 weeks prior if prolonged immobilisation expected after surgery (2) Discussion with patient and prescriber recommended.
Levothyroxine and anti-thyroid drugs	Carbimazole, levothyroxine, liothyronine, propylthiouracil	Continue	Consider checking TSH levels if not done within the last 12 months, or since change in dose (2).
Gastrointestinal			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Proton pump inhibitors	Esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole	Continue	(2)
H2 receptor antagonists	Famotidine, ranitidine, nizatidine	Continue	(2)
Anti-spasmodics, motility agents	Hyoscine butylbromide, mebeverine	Continue	(2)

Analgesics			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Nonsteroidal anti-inflammatory drugs (NSAIDs)	*COX-2 selective inhibitors:* Celecoxib, meloxicam, parecoxib *Non-selective COX inhibitors:* Aspirin (analgesic), diclofenac, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, naproxen, piroxicam	Generally continue unless high bleeding risk surgery If decision to omit prior to surgery, duration varies based on agent: - ibuprofen: 24 hrs - meloxicam: 5 days - all others 3 days	(2)
Opioids	Buprenorphine, fentanyl (including lozenges 'Actiq'; tablets 'Abstral' and 'Fentora'), morphine (Sevredol, MS Contin), oxycodone, Targin	Continue regular long-acting opioids. Established patches should be left on (7)	
Immunomodulators			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Biologic agents	Abatacept, adalimumab, anakinra, belimumab, etanercept, infliximab, rituximab, secukinumab, tocilizumab, ustekinumab *Targeted synthetic agents - JAK inhibitors*: baricitinib, tofacitinib	Withhold and plan surgery at the end of the dosing cycle for that medication (see Appendix B). Perioperative interruption requires consultation with the prescribing specialist.	These agents should not be restarted until external wound healing is complete. (15,16,17)
Disease modifying anti-rheumatic drugs (DMARDs)	Doxycycline, hydroxychloroquine, leflunomide, methotrexate, sulfasalazine	Continue	(15,16,17)

SLE-specific medications	Azathioprine, cyclosporin, mycophenolate, tacrolimus	Decision to withhold or continue is based on type of surgery and severity of disease, and should be made in conjunction with the patient's treating physician and proceduralist. In patients with severe disease, medication should be continued. If the decision is made to withhold, these medications should be ceased one week prior to surgery and only in consultation with prescribing specialist.	"Severe disease" is defined as: Currently treated for severe organ manifestations: lupus nephritis, central nervous system lupus, severe haemolytic anemia thrombocytopaenia, vasculitis (other than mild cutaneous vasculitis), including pulmonary hemorrhage, myocarditis, lupus pneumonitis, severe myositis (with muscle weakness, not just high enzymes), lupus enteritis (vasculitis), lupus pancreatitis, cholecystitis, lupus hepatitis, protein-losing enteropathy, malabsorption, orbital inflammation/myositis, severe keratitis, posterior severe uveitis/retinal vasculitis, severe scleritis, optic neuritis, anterior ischemic optic neuropathy (15,16,17)
Respiratory			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Inhaled bronchodilators (Beta 2 agonists and anticholinergics)	Salbutamol, ipratropium, tiotropium, glycopyrronium, umeclidinium	Continue	(2)
Inhaled corticosteroids	Beclomethasone, budesonide, ciclesonide, fluticasone	Continue	(2)
Xanthine derivatives	Theophylline	Continue	(2)
Other			
Class	**Examples**	**Continue/Omit**	**Notes (References)**
Anti-emetics	Metoclopramide, domperidone, ondansetron, prochlorperazine	Continue	
Antihistamines	*Sedating:* Alimemazine, cyclizine, cyproheptadine, dexchlorpheniramine, diphenhydramine, doxylamine, pheniramine, promethazine *Less sedating:* Cetirizine, desloratadine, fexofenadine, loratadine	Continue	

Erythropoiesis stimulating agents	Epoetins (Eprex, Neorecormon, Mircera); darbepoeitin (Aranesp)	Continue	
Herbal medications	Eg. Echinacea, fish oil, garlic, ginseng, glucosamine, krill oil, St John's Wort, turmeric	Omit 7 days prior to surgery	
Topical eye preparations		Continue	
Antiretrovirals (HIV agents)	*NRTI:* Abacavir, emtricitabine, lamivudine, zidovudine *NNRTI:* Efavirenz, etravirine *Protease inhibitors:* Darunavir, ritonavir *Integrase inhibitors:* Dolutegravir, raltegravir *Other:* Enfuviritide, maraviroc, tenofovir	Continue	Discuss with infectious disease specialist if a prolonged period of NBM is anticipated postoperatively

APPENDICES

Appendix A: Serotonergic agents

Appendix B: Immunomodulators

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General

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APPENDIX A: Serotonergic Agents

Serotonergic agents	
Increases serotonin formation	Tryptophan, oxitriptan
Increases release of serotonin	Amphetamines (including dextroamphetamine, methamphetamine) MDMA (ecstasy) Amphetamine derivatives (including fenfluramine, dexfenfluramine, phentermine) Cocaine Mirtazapine
Impairs serotonin reuptake from the synaptic cleft into the presynaptic neuron	Cocaine MDMA (ecstasy) Meperidine Tramadol Pentazocine Dextromethorphan Selective serotonin reuptake inhibitors (SSRIs; citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) Serotonin-norepinephrine reuptake inhibitors (SNRIs; desvenlafaxine, duloxetine, levomilnacipran, milnacipran, and venlafaxine) Sibutramine Bupropion Serotonin modulators (nefazodone, trazodone, vilazodone, and vortioxetine) Cyclic antidepressants (amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine) St. John's wort (Hypericum perforatum) 5-HT3 receptor antagonists (dolasetron, granisetron, ondansetron, palonosetron) Cyclobenzaprine Methylphenidate, dexmethylphenidate
Inhibits serotonin metabolism by inhibition of MAO	MAO inhibitors, nonselective (isocarboxazid, linezolid, phenelzine, Syrian rue [Peganum harmala, harmine], and tranylcypromine) MAO-A inhibitors (methylene blue, moclobemide) MAO-B inhibitors (rasagiline, safinamide, and selegiline)

Direct serotonin receptor agonist	Buspirone Triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) Ergot derivatives (including dihydroergotamine, ergotamine, methylergonovine) Fentanyl Lysergic acid diethylamide (LSD) Lasmiditan Lorcaserin Metaxalone
Increases sensitivity of postsynaptic serotonin receptor	Lithium

Bupropion inhibits neuronal uptake of dopamine and norepinephrine without known effects on serotonin; however, there have been case reports of serotonin syndrome when co-administered with other serotonergic drugs (eg. SSRIs); in some cases this may have been due to bupropion's inhibition of SSRI metabolism by CYP2D6.
Δ MAO selectivity is lost at higher doses and with drug interactions that increase serum drug concentrations. Inhibition of MAO-A is more likely to result in increased levels of serotonin within the CNS (ie, increased risk of serotonin syndrome) relative to MAO-B inhibition

(Ref. 2)

APPENDIX B: Immunomodulators:

American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline

DMARDs: CONTINUE these medications through surgery.	**Dosing Interval**	**Continue/Withhold**
Methotrexate	Weekly	Continue
Sulfasalazine	Once or twice daily	Continue
Hydroxychloroquine	Once or twice daily	Continue
Leflunomide (Arava)	Daily	Continue
Doxycycline	Daily	Continue
BIOLOGIC AGENTS: STOP these medications prior to surgery and schedule surgery at the end of the dosing cycle. RESUME medications at minimum 14 days after surgery in the absence of wound healing problems, surgical site infection, or systemic infection.	**Dosing Interval**	**Schedule Surgery (relative to last biologic agent dose administered) during**
Adalimumab (Humira)	Weekly or every 2 weeks	Week 2 or 3
Etanercept (Enbrel)	Weekly or twice weekly	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5 Week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4-6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2 Week 5
Anakinra (Kineret)	Daily	Day 2
Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Belimumab (Benlysta)	Every 4 weeks	Week 5
Tofacitinib (Xeljanz): STOP this medication 7 days prior to surgery.	Daily or twice daily	7 days after last dose
SEVERE SLE-SPECIFIC MEDICATIONS: CONTINUE these medications in the perioperative period.	**Dosing Interval**	**Continue/Withhold**
Mycophenolate mofetil	Twice daily	Continue
Azathioprine	Daily or twice daily	Continue
Cyclosporine	Twice daily	Continue
Tacrolimus	Twice daily (IV and PO)	Continue
NOT-SEVERE SLE: DISCONTINUE these medications 1 week prior to surgery	**Dosing Interval**	**Continue/Withhold**
Mycophenolate mofetil	Twice daily	Withhold
Azathioprine	Daily or twice daily	Withhold
Cyclosporine	Twice daily	Withhold
Tacrolimus	Twice daily (IV and PO)	Withhold

(Ref. 16)