

# Preoperative Management of Gastrointestinal and Pulmonary Medications: Society for Perioperative Assessment and Quality Improvement (SPAQI) Consensus Statement

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## Abstract

Perioperative medication management is integral to preoperative optimization but remains challenging because of a paucity of literature guidance. Published recommendations are based on the expert opinion of a small number of authors without collaboration from multiple specialties. The Society for Perioperative Assessment and Quality Improvement (SPAQI) recognized the need for consensus recommendations in this area as well as the unique opportunity for its multidisciplinary membership to fill this void. In a series of articles within this journal, SPAQI provides preoperative medication management guidance based on available literature and expert multidisciplinary consensus. The aim of this consensus statement is to provide practical guidance on the preoperative management of gastrointestinal and pulmonary medications. A panel of experts with anesthesiology, perioperative medicine, hospital medicine, general internal medicine, and medical specialty experience was drawn together and identified the common medications in each of these categories. The authors then used a modified Delphi approach to review the literature and to generate consensus recommendations.

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Medication management is key to optimizing the care of patients undergoing invasive procedures. Clinicians must ascertain whether a patient's long-term medications may alter anesthetic or analgesic effects or increase surgery- or anesthesia-related bleeding risk. Common postoperative complications, including postoperative delirium and respiratory depression, may also be increased by some medications. However, inappropriate withholding of medications is equally important because of the risks associated with systemic disease and medication withdrawal syndromes. Further complicating management is the fact that surgery type must also be factored into decision-making. For some medications, outcomes with one type of surgery may be minimally affected, whereas complications are increased for another.

Thus, close collaboration with proceduralists and specialists is imperative.

Continuous evolution of anesthetic and surgical practices and US Food and Drug Administration (USFDA)—approved therapies complicates the process of perioperative medication management. Coupled with a shortage of evidence-based resources, clinicians lack guidance for optimal practice. The Society for Perioperative Assessment and Quality Improvement (SPAQI) seeks to fill this practice gap by leveraging its specialized focus in the field of perioperative medicine.

SPAQI is an international, multidisciplinary society dedicated to the promotion of evidence-based perioperative medicine and has produced a number of recommendation papers and consensus statements in this field.<sup>1-3</sup> SPAQI drafted a comprehensive plan

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for developing consensus recommendations for preoperative medication management using perioperative medicine, anesthesiology, internal medicine, hospital medicine, and medical subspecialty experts. This consensus statement contains the work of a subgroup focused on providing guidance on the preoperative management of gastrointestinal and pulmonary medications.

## METHODS

Subject matter for the SPAQI consensus statements was selected by SPAQI leadership on the basis of knowledge and practice gaps identified from discussions with the membership. Gastrointestinal and pulmonary medications were combined for this consensus group to balance the volume of information across the series of recommendation statements. Members of the consensus group were recognized experts in the fields of perioperative medicine, anesthesiology, general internal medicine, hospital medicine, and subspecialty internal medicine from several different academic institutions.

The group first identified common USFDA-approved medications for pulmonary and gastrointestinal disease. Medications and supplements without USFDA-approved indications were not included in our review. Using a modified Delphi methodology described in the first publication of SPAQI's series of medication consensus statements, the group conducted consensus determination meetings and reviewed available literature.<sup>2</sup> Literature reviews were independently conducted through PubMed queries with relevant search terms by at least 3 different members of the group and findings shared with the whole group for discussion. From this process, the group derived consensus recommendations using the following guiding principles:

- Preference is given to not interrupting therapy unless there are potential risks from continuation.
- Focus is placed on management of long-term medications.
- Preoperative initiation of therapy, supplemental treatment (eg, "stress dose steroids"),

and postoperative management are outside the scope of this paper.

- Long-term oral corticosteroid management is covered in another publication within this series, entitled "Preoperative Management of Endocrine, Hormonal, and Urologic Medications: Society for Perioperative Assessment and Quality Improvement (SPAQI) Consensus Statement."<sup>3</sup>

Consensus was established for all reviewed medications, and the completed set of recommendations was reviewed and approved by the Executive Committee of SPAQI. Described here are specific recommendations for each medication class.

## PULMONARY MEDICATIONS

Recommendations for the preoperative management of pulmonary medications are summarized in [Table 1](#).

### Anticholinergic Medications

These inhaled medications work by blocking the ability of acetylcholine to bind to muscarinic receptors, in turn inhibiting bronchial constriction and mucus production. Specific drugs in this class include ipratropium, tiotropium, aclidinium, umeclidinium, revefenacin, and inhaled glycopyrrolate. Minimal literature about perioperative management of inhaled anticholinergics is available, but at least 2 studies found lower rates of pulmonary complications in patients using inhaled tiotropium (alone or in combination with formoterol and budesonide) preoperatively.<sup>4</sup>

*Consensus Recommendation:* Continue inhaled anticholinergic medications up to and including the day of surgery.

### $\beta_2$ -Adrenergic Agonists

The  $\beta_2$ -adrenergic agonists activate cyclic adenosine monophosphate, causing relaxation of smooth muscles and improved airway flow. Medications in this class include inhaled agents that are short-acting (albuterol, metaproterenol, and levalbuterol) and long-acting (salmeterol, formoterol, aformoterol, indacaterol, and olodaterol). There is no specific evidence of perioperative adverse events related to these medications, and in

TABLE 1. Summary of Recommendations for the Preoperative Management of Pulmonary Medications

Medication class	Examples	Management before the morning of surgery	Management on the morning of surgery	Additional considerations
Anticholinergics, inhaled	Ipratropium, tiotropium, aclidinium, umeclidinium, revefenacin, glycopyrrolate	Continue	Continue	Same instructions if part of a combination inhaler
Antifibrotic medications	Nintedanib, pirfenidone	Continue	Continue	Discuss perioperative management with prescribing clinician because of potential for inhibited wound healing
Arylalkylamine decongestants	Phenylephrine, pseudoephedrine	Continue	Hold	
$\beta_2$ -Adrenergic agonists	Albuterol, metaproterenol, levalbuterol, salmeterol, formoterol, afomoterol, indacaterol, olodaterol, vilanterol	Continue	Continue	Same instructions if part of a combination inhaler
Corticosteroids, inhaled	Fluticasone, budesonide, mometasone, beclomethasone	Continue	Continue	Same instructions if part of a combination inhaler
Endothelin receptor antagonists	Bosentan, macitentan, ambrisentan	Continue	Continue	<ul style="list-style-type: none"> <li>• Potential for rebound PH with discontinuation</li> <li>• Can cause adverse effects of fluid retention, edema, anemia</li> <li>• Bosentan is a CYP3A4 inducer; concomitant use with opioids decreases opioid efficacy; may require higher opioid doses for pain control</li> <li>• Bosentan and macitentan have drug-drug interactions with erythromycin, clarithromycin, amiodarone, diltiazem, verapamil, itraconazole, fluconazole, and others that increase the plasma levels of the endothelin receptor antagonist</li> <li>• Preoperative studies: CBC (for all) and hepatic function tests (for bosentan and macitentan)</li> <li>• Coordinate perioperative care with prescribing clinician</li> </ul>
H <sub>1</sub> antihistamines	Hydroxyzine, dimenhydrinate, cetirizine, diphenhydramine, loratadine, levocetirizine, fexofenadine, desloratadine	Continue	Hold (see additional considerations)	Hold first-generation antihistamines and cetirizine on the day of surgery because of their potential for contributing to postoperative delirium and anticholinergic adverse effects
Leukotriene inhibitors	Montelukast, zafirlukast, zileuton	Continue	Continue	Concurrent use of zileuton and beta blockers may result in a significant increase in $\beta$ -adrenergic blockade; concurrent use with amiodarone, clarithromycin, and fluconazole increases the risk of zileuton toxicity
N-Acetylcysteine		Continue	Continue	Concurrent use with nitroglycerin can result in enhanced hypotension and increased headache
PDE-4 inhibitor	Roflumilast	Continue	Continue	Concurrent use with erythromycin, clarithromycin, fluconazole, or cimetidine may result in increased roflumilast exposure and risk for toxicity

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TABLE 1. Continued

Medication class	Examples	Management before the morning of surgery	Management on the morning of surgery	Additional considerations
PDE-5 inhibitors	Sildenafil, tadalafil	Continue	Continue	<ul style="list-style-type: none"> <li>● Recommendation is for use for PH</li> <li>● If used for urologic indication, hold for 3 days before surgery</li> <li>● Metabolized by CYP3A4; concurrent use with erythromycin, azithromycin, ciprofloxacin, or -azole antifungals increases risk of hypotension, headache, and visual changes from PDE-5 inhibitors</li> <li>● Coordinate perioperative care with prescribing clinician</li> </ul>
Prostacyclin analogues	Epoprostenol, treprostinil, iloprost	Continue	Continue	<ul style="list-style-type: none"> <li>● Dangerous to interrupt therapy because of rebound PH; ensure adequate preparation for continuous administration perioperatively</li> <li>● Increased risk of hemorrhagic complications due to antiplatelet effects, particularly when used concurrently with anticoagulants and other antiplatelet agents</li> <li>● Coordinate perioperative care with prescribing clinician</li> </ul>
Riociguat		Continue	Continue (see additional considerations)	<ul style="list-style-type: none"> <li>● Discuss potential for bleeding complications with the surgeon or proceduralist</li> <li>● Concurrent use with nitrates is contraindicated because of risk for significant hypotension</li> <li>● Concurrent use with clarithromycin or itraconazole increases riociguat levels and risk of hypotension</li> <li>● Coordinate perioperative care with prescribing clinician</li> </ul>
Selexipag		Continue	Continue	<ul style="list-style-type: none"> <li>● Increased risk of hemorrhagic complications, particularly with concurrent use of other antiplatelet agents or anticoagulants</li> <li>● Preoperative studies: CBC</li> <li>● Coordinate perioperative care with prescribing clinician</li> </ul>
Theophylline		Continue	Hold	<ul style="list-style-type: none"> <li>● Consider discussion of long-term necessity with the prescriber because of narrow therapeutic window, potential for drug interactions, and cardiac adverse effects</li> <li>● Concurrent use with ciprofloxacin, erythromycin, clarithromycin, cimetidine, ranitidine, fluconazole, imipenem, or levofloxacin may result in theophylline toxicity (nausea, vomiting, palpitations, seizures)</li> <li>● Theophylline can decrease the effectiveness of benzodiazepines and pancuronium</li> </ul>

CBC, complete blood count; PDE-4, phosphodiesterase type 4; PDE-5, phosphodiesterase type 5; PH, pulmonary hypertension.

a randomized trial with patients undergoing esophagectomy, salmeterol started immediately before surgery was associated with a significant decrease in pneumonia incidence.<sup>5</sup>

*Consensus Recommendation:* Continue inhaled  $\beta_2$ -adrenergic agonists up to and including the day of surgery.

### Theophylline

Theophylline is an orally administered 3-methylxanthine presumed to induce airway smooth muscle relaxation through inhibition of phosphodiesterase (PDE). Inhibition of PDE type 3 accounts for most of its bronchodilator effects, although it may also have anti-inflammatory effects. Cardiac adverse effects, drug interactions, and a narrow therapeutic window have led to drastically decreased use. We could identify no relevant literature guiding its preoperative management, but the negative aspects causing its decline in general use also raise concern for its perioperative administration.

*Consensus Recommendations:* Continue theophylline before the day of surgery but hold on the day of surgery because of its narrow therapeutic window, potential for drug interactions, and cardiac adverse effects. Consider discussion of long-term necessity with the prescriber.

### Roflumilast

This inhaled medication inhibits PDE type 4, leading to reduction of inflammatory mediators. It has been reported to increase lung function and to decrease exacerbations of chronic obstructive pulmonary disease (COPD) in patients already using other guideline-directed therapies.<sup>6</sup> There is no specific literature on the perioperative management of roflumilast, but there are also no serious adverse effects to warrant interruption of this therapy that improves pulmonary function.

*Consensus Recommendation:* Continue roflumilast up to and including the day of surgery.

### Inhaled Corticosteroids

Inhaled corticosteroids decrease airway inflammation and hyperreactivity and are a cornerstone for treatment of obstructive

lung disease. Oral steroids cause many undesirable adverse effects, including adrenal suppression, bone demineralization, and immunosuppression, but the systemic impact of inhaled corticosteroids remains relatively low except when they are used at the highest dosages.<sup>7</sup> Specifically, there is no evidence of perioperative harm from use of inhaled corticosteroids, and some evidence suggests benefit from preoperative use.<sup>8,9</sup>

*Consensus Recommendation:* Continue inhaled corticosteroids up to and including the day of surgery.

### Combination Inhaled Medications

Multiple USFDA combinations of inhaled corticosteroids, long-acting  $\beta_2$  agonists, and anticholinergics are available for treatment of asthma and COPD. Literature specific to these products is included in the preceding sections.

*Consensus Recommendation:* Continue combination inhaled medications up to and including the day of surgery.

### Leukotriene Inhibitors

Montelukast, zafirlukast, and zileuton are oral asthma medications that exert their therapeutic effect by blocking leukotriene-mediated inflammation. There is no specific literature about the perioperative use of these medications, but their adverse effect profile does not include elements that would preclude their use before surgery.

*Consensus Recommendation:* Continue leukotriene inhibitors up to and including the day of surgery.

### N-Acetylcysteine

N-Acetylcysteine is used for some patients with COPD to thin respiratory secretions and potentially to reduce the frequency of exacerbations. Given its relatively low incidence of serious adverse effects and the lack of literature about its perioperative use, continuation of therapy through surgery is appropriate.

*Consensus Recommendation:* Continue N-acetylcysteine up to and including the day of surgery.

### H<sub>1</sub> Antihistamines

Medications from this class include both first-generation H<sub>1</sub> antihistamines and second-generation H<sub>1</sub> antihistamines (cetirizine, levocetirizine, fexofenadine, desloratadine, and loratadine); they are used for several purposes, such as allergic rhinosinusitis, atopic dermatitis, insomnia, and anxiety. First-generation H<sub>1</sub> antihistamines penetrate the blood-brain barrier (which may cause somnolence) and also have anticholinergic adverse effects. For these reasons, their use is discouraged in elderly patients in all situations but particularly around surgery because they may contribute to perioperative neurocognitive dysfunction.<sup>10,11</sup> Second-generation H<sub>1</sub> antihistamines do not have anticholinergic effects and, with the exception of cetirizine, do not have central nervous system penetrance.<sup>12</sup>

*Consensus Recommendation:* Continue antihistamines before the day of surgery but hold first-generation antihistamines and cetirizine on the day of surgery because of their potential for contributing to postoperative delirium and anticholinergic adverse effects.

### Arylalkylamine Decongestants

These medications, including phenylephrine and pseudoephedrine, are available over-the-counter remedies for symptomatic relief of rhinitis. Decongestants are sympathomimetic, and a major adverse effect is elevated blood pressure. No perioperative studies of these medications are available, but given their noncritical use and their potential cardiovascular effects, withholding immediately before surgery is warranted.

*Consensus Recommendation:* Continue arylalkylamine decongestants before the day of surgery but hold on the day of surgery because of their potential for contributing to cardiovascular adverse effects.

### Medications for Pulmonary Hypertension

Patients who require medication treatment for pulmonary hypertension (PH; primarily group 1 PH, pulmonary arterial hypertension) have substantial and unique perioperative risks requiring specialized knowledge

and expertise. For all such patients, preoperative optimization must include collaboration with anesthesia providers and the patient's PH specialist and assurance that the procedure is being performed in a facility with appropriate experience and resources for managing PH.<sup>13</sup> The following recommendations are for general guidance and should not replace consultation with PH specialists and anesthesiologists.

**Prostacyclin Analogues.** Medications in this class include epoprostenol, treprostinil, and iloprost and produce pulmonary vasodilation through stimulation of adenylate cyclase. Epoprostenol is given intravenously and has a half-life of 3 to 5 minutes. Iloprost also has a short half-life (~30 minutes) and can be given intravenously or inhaled. Treprostinil has a half-life of approximately 4 hours and can be given orally, intravenously, inhaled, or subcutaneously. Uninterrupted continuation of these medications is critical because not doing so can lead to acute right-sided heart failure and death.<sup>14</sup> Given the potential cardiovascular risks and special considerations for equipment and training for managing these medications, we advise consulting with the anesthesiology service as far in advance of surgery as possible, especially if the patient is on a continuous infusion.

*Consensus Recommendations:* Continue prostacyclin analogues up to and including the day of surgery.

**Selexipag.** Selexipag is a selective prostacyclin receptor agonist that is administered orally and is long-acting (half-life of ~6 to 12 hours). Its mechanism of action and adverse effect profile are similar to those of prostacyclin analogues. Although selexipag's longer half-life leads to less risk for sudden cardiovascular decompensation with withdrawal of the drug, its importance in managing PH necessitates its perioperative continuation.<sup>15</sup>

*Consensus Recommendations:* Continue selexipag up to and including the day of surgery.



**Endothelin Receptor Antagonists.** Endothelin 1 is a polypeptide responsible for potent and long-lasting vasoconstriction, and its effects are mediated through 2 receptors, endothelin A and endothelin B. Medications in this class, including bosentan, macitentan, and ambri-sentan, are orally administered. Macitentan and bosentan are antagonists for both endothelin A and endothelin B, whereas ambri-sentan is an endothelin A-selective antagonist. There is a paucity of data on perioperative management of these medications, but their continuation is advised, given their importance in the management of PH.

*Consensus Recommendations:* Continue endothelin receptor antagonists up to and including the day of surgery.

**Phosphodiesterase Type 5 (PDE-5) Inhibitors.** Sildenafil and tadalafil are medications in this class used for PH. These medications lead to direct myocardial effects through cyclic guanosine monophosphate and cyclic adenosine monophosphate activation that may counterbalance hypertrophic and proapoptotic signaling, including adrenergic stimulation.<sup>16</sup> Minimal data on perioperative management of PDE-5 inhibitors for PH are available. They are less likely than prostacyclin analogues to cause a pulmonary hypertensive crisis with interruption, but they should be continued because of the importance of adequately treated PH.

*Consensus Recommendations:* Continue PDE-5 inhibitors up to and including the day of surgery when used for treatment of PH. Perioperative management of PDE-5 inhibitors prescribed for urologic indications is detailed in another publication within this consensus statement series.<sup>3</sup>

**Riociguat.** Riociguat is an oral PH medication that works by stimulating soluble guanylate cyclase, which induces vasodilation in vascular smooth muscle and assists in reducing elevated pulmonary pressure. It is the only PH medication that is USFDA approved for treatment of group 4 PH (due to chronic thromboembolic disease). At grossly suprathreshold doses, riociguat inhibits platelet function, and nonsurgical

bleeding complications have been described with this drug.<sup>17,18</sup> We identified no specific perioperative literature for riociguat. Because this medication is not associated with a severe withdrawal syndrome, interruption could be considered in select cases when surgical bleeding risk is particularly high.<sup>18</sup>

*Consensus Recommendations:* Continue riociguat up to and including the day of surgery, but discuss potential for bleeding complications with the surgeon or proceduralist.

### Antifibrotic Medications

As of publication of this manuscript, 2 medications are USFDA approved for treatment of idiopathic pulmonary fibrosis (IPF): nintedanib and pirfenidone. Pirfenidone reduces fibroblast proliferation and inhibits collagen formation. Nintedanib is a small-molecule tyrosine kinase inhibitor that impedes pulmonary fibrosis and has been found to improve quality of life and lung function in patients with IPF and other progressive pulmonary fibrosis conditions. Pirfenidone may cause hepatotoxic effects and is metabolized through CYP1A2, which could lead to toxicity of medications affecting this enzymatic pathway (eg, fluconazole, ciprofloxacin, paroxetine). Nintedanib is associated with increased risk of arterial thromboembolism, hepatotoxicity, and bleeding. Given their antifibrotic properties, concerns of impaired wound healing have been raised. Although one recent case report described wound dehiscence associated with nintedanib use after cardiac surgery, other literature found no apparent increased wound complications and fewer than expected IPF exacerbations in lung transplant patients receiving nintedanib and pirfenidone.<sup>19-21</sup> A phase 2 trial of perioperative administration of pirfenidone to surgical patients with lung cancer also found no apparent increase in wound or bleeding complications but decreased acute exacerbations of IPF.<sup>22</sup> Given these potential perioperative benefits, continuing these medications uninterrupted through other types of surgery is worth discussing with patients' surgeons and specialty clinicians.

*Consensus Recommendations:* Continue nintedanib and pirfenidone up to and including the day of surgery, but discuss perioperative management with the surgeon and prescribing clinician.

## GASTROINTESTINAL MEDICATIONS

Recommendations for the preoperative management of gastrointestinal medications are summarized in [Table 2](#).

### Proton Pump Inhibitors

Proton pump inhibitors (PPIs) block gastric acid production by inhibiting the hydrogen-potassium ATPase pump on the parietal cell membrane. They are used for treating gastroesophageal reflux disease, peptic ulcer disease, Zollinger-Ellison syndrome, nonsteroidal anti-inflammatory drug–related ulcerations, and *Helicobacter pylori* infection.

Despite limited data to support the practice, gastric acid suppression is often used as a means of preventing anesthesia-related aspiration.<sup>23,24</sup> However, the American Society of Anesthesiologists does not recommend routinely providing pharmacologic blockade of gastric acid secretion for this purpose.<sup>25</sup> Complications of PPIs not specifically studied in the surgical setting but consequential to the perioperative setting include hypomagnesemia leading to increased arrhythmogenic potential and iron and vitamin B<sub>12</sub> malabsorption leading to anemia. Because PPIs are extensively metabolized through CYP450, important drug-drug interactions with medications such as warfarin, benzodiazepines, and many others increase the risk of toxicity or decrease the efficacy of these drugs. The PPIs also decrease the antiplatelet efficacy of clopidogrel.<sup>26</sup> Whereas these effects are important considerations, there are no data suggesting specific perioperative risks, and the potential benefits of continuation include prevention of peptic ulcer and gastroesophageal disease, which can be serious postoperative complications.

*Consensus Recommendation:* Continue PPIs up to and including the day of surgery.

### H<sub>2</sub> Receptor Antagonists

H<sub>2</sub> receptor antagonists block acid secretion on the gastric parietal cell surface. This class of drugs is thought to be safe overall perioperatively. However, early literature in cardiac surgery suggested no benefit in raising gastric pH and possible stomach colonization associated with a trend toward increased nosocomial pneumonia.<sup>27</sup> Furthermore, some authors have postulated a risk of possible central nervous system effects and postoperative delirium on the basis of limited data.<sup>11,12</sup> These medications are metabolized by cytochrome P450 pathways and therefore can cause drug interactions. Famotidine has been reported to prolong QT interval and can increase the risk of arrhythmias when it is used with other drugs that also prolong QT.<sup>28</sup> Ranitidine was pulled from the market by the USFDA in April 2020 because of concerns about a contaminant, N-nitrosodimethylamine, identified in some ranitidine products that were stored at higher than room temperatures over time.<sup>29</sup> The H<sub>2</sub> blockers are renally excreted and require a dose reduction or longer dosing interval if the creatinine clearance drops below 50 mL/min. Rapid infusion of these agents can cause cardiac effects including bradycardia, heart block, and QT prolongation, but this is rare. Similar to PPIs, these potential adverse effects are important; but for patients who tolerate these therapies long term without problems, perioperative continuation is reasonable to maintain treatment of gastrointestinal disease that could cause postoperative complications if it is inadequately treated.

*Consensus Recommendation:* Continue H<sub>2</sub> receptor antagonists up to and including the day of surgery.

### Antacids

Antacid formulations are commonly composed of sodium citrate, magnesium trisilicate, aluminum hydroxide, calcium carbonate, or sucralfate. They neutralize gastric acid directly and diminish acid delivery to the duodenum. The American Society of



TABLE 2. Summary of Recommendations for the Preoperative Management of Gastrointestinal Medications

Medication class	Examples	Management before the morning of surgery	Management on the morning of surgery	Additional considerations
5-Aminosalicylic acid	Mesalamine, balsalazide, olsalazine, sulfasalazine	Continue	Continue	<ul style="list-style-type: none"> <li>Consider holding on the morning of surgery if GFR &lt;50 mL/min</li> <li>Preoperative studies: CBC and creatinine</li> </ul>
5-HT <sub>3</sub> antagonists	Ondansetron, granisetron, dolasetron, palonosetron	Continue	Continue	<ul style="list-style-type: none"> <li>Prolong QT interval</li> <li>Caution with concurrent use with other serotonergic drugs; can increase risk of serotonin syndrome</li> </ul>
Antacids	Sodium citrate, magnesium trisilicate, aluminum hydroxide, calcium carbonate, sucralfate	Continue	Hold	Nonparticulate antacids (sodium citrate and magnesium trisilicate) may be acceptable to take on the morning of surgery for patients at increased risk for pulmonary aspiration
Anticholinergics or antispasmodics	Dicyclomine, hyoscyamine	Continue	Hold	Reexamine the long-term necessity of these medications (especially in elderly patients); if absolutely needed for airway secretion control that could affect airway management, continuation of these agents is reasonable
Antidiarrheals	Loperamide, diphenoxylate, atropine	Continue	Hold	
Anti-HBV reverse transcriptase inhibitors	Entecavir, tenofovir, lamivudine, adefovir	Continue	Continue	<ul style="list-style-type: none"> <li>Consult with the prescribing clinician</li> <li>Preoperative studies: creatinine and hepatic function studies</li> </ul>
Aprepitant		Continue	Continue	<ul style="list-style-type: none"> <li>Concomitant use with hormonal contraceptives may decrease efficacy during therapy and for 28 days after therapy</li> <li>Concurrent use with opioids or midazolam can increase risk of respiratory depression and opioid toxicity</li> </ul>
Bupropion/naltrexone		Hold for 72 hours before surgery	Hold	If procedure will not require opioid use, may be reasonable to continue uninterrupted
Dasabuvir/ombitasvir/paritaprevir/ritonavir		Continue	Hold	Discuss management with prescribing clinician
Dopamine antagonist antiemetics	Promethazine, prochlorperazine, droperidol, metoclopramide	Continue	Continue	<ul style="list-style-type: none"> <li>Multiple drug-drug interactions</li> <li>Use with caution in patients with QT prolongation; avoid concurrent use with other QT-prolonging medications</li> <li>Caution with concurrent use of central nervous system depressant medications because of increased risk of respiratory depression</li> <li>Avoid use in patients with COPD and sleep apnea because of increased risk of potentially fatal respiratory depression</li> <li>Avoid use in patients with Parkinson disease and in elderly with increased risk of delirium because of significant anticholinergic effects</li> <li>Preoperative studies: ECG</li> </ul>

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TABLE 2. Continued

Medication class	Examples	Management before the morning of surgery	Management on the morning of surgery	Additional considerations
Elbasvir/grazoprevir		Continue	Hold	Discuss management with prescribing clinician
Gallstone solubilizing agents	Ursodiol, chenodeoxycholic acid	Continue	Hold	
Glecaprevir/pibrentasvir		Continue	Hold	Discuss management with prescribing clinician
Guanylate cyclase C agonists	Linaclotide, plecanatide	Continue	Continue	
H <sub>2</sub> antagonists	Ranitidine, famotidine	Continue	Continue	<ul style="list-style-type: none"> <li>• H<sub>2</sub> antagonists may induce or worsen delirium in elderly patients</li> <li>• Famotidine increases QT interval; concurrent use with other medications that also prolong QT increases risk of arrhythmias</li> <li>• Cimetidine is associated with multiple drug interactions, causing increased toxicity and adverse effects of several beta blockers, calcium channel blockers, benzodiazepines, warfarin, lidocaine, tramadol, morphine, and oxymorphone</li> <li>• Concurrent use of cimetidine (CYP2D6 inhibitor) with tramadol increases plasma concentrations of tramadol (increased seizures, serotonin syndrome) and decreases levels of the active metabolite M1 (reduced efficacy for pain control)</li> </ul>
Laxatives	Senosides, PEG 3350, bisacodyl, magnesium citrate/hydroxide, lactulose, docusate sodium	Continue	Hold	
Ledipasvir/sofosbuvir		Continue	Continue	<ul style="list-style-type: none"> <li>• Discuss with gastroenterologist whether it is optimal to delay surgery until completion of therapy</li> <li>• Coadministration with amiodarone can result in significant bradycardia</li> </ul>
Liraglutide		Continue (see additional considerations)	Hold	<p>Before day of surgery: For gastrointestinal surgery or when there is concern for nausea, vomiting, or gut dysfunction, consider holding weekly dose within 7 days before surgery</p> <p>Day of surgery: If weekly dose is due on morning of surgery, delay until later in day after surgery is complete</p>
Lisdexamfetamine		Hold for 72 hours before surgery	Hold	For patients at high risk for relapse of binge eating disorder, may continue before surgery and hold only on morning of surgery, but this requires discussion with the prescriber and anesthesiologist
Lubiprostone		Continue	Continue	
Orlistat		Continue	Hold	
Pancreatic enzymes	Pancrelipase	Continue	Hold	

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TABLE 2. Continued

Medication class	Examples	Management before the morning of surgery	Management on the morning of surgery	Additional considerations
Pegylated interferons	Pegylated interferon alfa-2a, pegylated interferon alfa-2b	When used for treatment of viral hepatitis, stop interferons 1-2 weeks before surgery because of potential for perioperative complications	Hold	<ul style="list-style-type: none"> <li>Consult with the prescribing clinician</li> <li>Preoperative studies: CBC, basic metabolic panel, thyroid-stimulating hormone, hepatic function studies, ECG</li> </ul>
Phentermine		Hold for at least 4 days before surgery	Hold	
Phentermine/topiramate		Hold for at least 4 days before surgery (see additional considerations)	Hold	<ul style="list-style-type: none"> <li>Either wean the patient off during the course of a week before surgery (according to product insert) or, while withholding, provide topiramate alone at the same dose</li> <li>Preoperative studies: bicarbonate, potassium, creatinine, and glucose</li> </ul>
Proton pump inhibitors	Pantoprazole, omeprazole, lansoprazole, esomeprazole, dexlansoprazole	Continue	Continue	
Ribavirin		Continue	Hold	Preoperative studies: CBC
Serotonergic neuroenteric modulators	Tegaserod, alosetron, prucalopride	Continue	Continue	
Sofosbuvir		Continue	Continue	<ul style="list-style-type: none"> <li>Discuss with patient's gastroenterology clinician whether it is optimal to delay surgery until completion of therapy</li> <li>Coadministration with amiodarone can result in significant bradycardia</li> </ul>
Sofosbuvir/velpatasvir		Continue	Hold	Discuss management with prescribing clinician
Sofosbuvir/velpatasvir/voxilaprevir		Continue	Hold	Discuss management with prescribing clinician

CBC, complete blood count; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; GFR, glomerular filtration rate; HBV, hepatitis B virus; PEG, polyethylene glycol; 5-HT<sub>3</sub>, 5-hydroxytryptamine receptor 3.

Anesthesiologists recommends against routine preoperative use of antacids and strongly recommends against the use of particulate antacids (aluminum hydroxide, calcium carbonate, or sucralfate), which are associated with a higher risk and severity of aspiration events.<sup>25</sup> For patients at increased risk for pulmonary aspiration, nonparticulate antacids (sodium citrate and magnesium trisilicate) may be considered for their potential to reduce aspiration-related complications.<sup>25</sup>

*Consensus Recommendations:* Continue antacids up to the day before surgery but hold on the morning of surgery. Nonparticulate antacids may be acceptable to take on the morning of surgery for patients at increased risk for pulmonary aspiration.

**Antiemetics**  
**5-Hydroxytryptamine Receptor 3 (5-HT<sub>3</sub>) Antagonists.** These agents are commonly used for control of nausea and vomiting in

the perioperative period and in cancer patients and exert their effect by antagonizing 5-HT<sub>3</sub> receptors centrally in the chemoreceptor trigger zone. Four 5-HT<sub>3</sub> antagonists are approved by the FDA; they are ondansetron, granisetron, dolasetron, and palonosetron. These medications are well tolerated with few adverse effects. However, caution is advised when these medications are used concurrently with medications that prolong QT interval (torsades de pointes) or have serotonergic properties (serotonin syndrome).

*Consensus Recommendation:* Continue 5-HT<sub>3</sub> antagonists up to and including the day of surgery.

**Dopamine Antagonists.** Promethazine, prochlorperazine, droperidol, and metoclopramide are centrally acting dopamine antagonists that are effective for treatment of nausea and vomiting in multiple settings. Metoclopramide is also used as a gastrointestinal stimulant to improve gastric emptying and bowel motility. Available data suggest that these medications are safe in the perioperative period; however, their antidopaminergic effect may lead to extrapyramidal symptoms, neuroleptic malignant syndrome, and tardive dyskinesia (with prolonged therapy), and they can prolong the QT interval. These drugs have multiple drug-drug interactions with many medications; it may be beneficial to consult with a pharmacist if these medications are prescribed throughout the postoperative period.

*Consensus Recommendation:* Continue dopamine antagonists up to and including the day of surgery, unless there are concerns of significant QT prolongation.

**Aprepitant.** Aprepitant is a neurokinin 1 antagonist that is a highly effective and costly oral antiemetic. It is well tolerated and has been found to be safe and effective in the perioperative setting.<sup>30</sup> Concurrent use of aprepitant with opioids, midazolam, alprazolam, or triazolam can increase risk of respiratory depression and opioid toxicity, but this is less of a concern if a single dose is used. It has also been reported to decrease

the efficacy of oral contraceptive medications for up to 28 days; it is important to mention to women that an alternative form of contraception should be used for 1 month after the last dose of aprepitant. Aprepitant is a substrate, inhibitor, and inducer of CYP3A4 and an inducer of CYP2C9, so there are drug-drug interactions to be aware of if this medication is used consistently.<sup>31</sup>

*Consensus Recommendation:* Continue aprepitant up to and including the day of surgery.

### Hepatitis B and C Antivirals

For all patients undergoing therapy for eradication or suppression of hepatitis B virus (HBV) or hepatitis C virus (HCV), the preoperative care clinician should discuss perioperative management with patients' gastroenterology clinicians. Specifically, it should be determined whether a patient's liver disease is sufficiently optimized to tolerate surgery and whether a nonurgent procedure should be delayed to allow the completion of eradication therapy.

**Anti-HBV Reverse Transcriptase Inhibitors.** Entecavir, tenofovir, and lamivudine are used in the treatment of chronic HBV infection as well as HBV and human immunodeficiency virus (HIV) co-infection. Entecavir and lamivudine are nucleoside reverse transcriptase inhibitors; tenofovir is a nucleotide reverse transcriptase inhibitor. Adefovir is another nucleotide reverse transcriptase inhibitor that is rarely used and effective only for chronic HBV infection. All these medications inhibit HBV replication but do not completely eliminate the virus; thus, these agents are usually taken indefinitely. All are also associated with potential nephrotoxicity, which should be taken into consideration for patients with alterations in renal function. Although HBV recurrence from brief withholding is unlikely, no specific perioperative adverse effects have been identified that would suggest a need to stop these medications. Some evidence suggests benefit from preoperative use of entecavir in patients undergoing HBV-associated hepatocellular carcinoma resection.<sup>32</sup>

*Consensus Recommendations:* Continue entecavir, tenofovir, lamivudine, and adefovir up to and including the day of surgery but consult with the prescribing clinician. Assess renal and hepatic function before surgery because of nephrotoxicity and hepatotoxicity of these agents.

**Pegylated Interferons.** Pegylated interferon alfa-2a is a rarely used monotherapy for hepatitis B. Pegylated interferon alfa-2a and pegylated interferon alfa-2b may be used in combination with oral antivirals for treatment of hepatitis C. The antiviral mechanisms of interferons are immunoregulatory and complex. Unlike oral antivirals, these subcutaneous medications are administered for a defined time (24 to 48 weeks) and have the advantage of long-term sustained virologic response (20% to 30% for HBV and 40% to 60% for HCV). The potential adverse effects of interferons are well documented and common; they include immunologic, hematologic, metabolic, neuropsychiatric, and pulmonary complications. Because of these adverse effects and the efficacy of oral therapies, interferons are rarely used in the treatment of viral hepatitis. Perioperative safety data are lacking, but these drugs have metabolism interactions with opioids and lidocaine that raise concerns for their perioperative use. Based on their adverse effect profile, withholding of anti-HBV or anti-HCV interferon therapy before surgery would appear prudent. Because use of interferons for hepatitis treatment is unusual, decision-making for perioperative interferon management should be discussed in detail with the gastroenterology team.

*Consensus Recommendations:* When interferons are used for treatment of viral hepatitis, stop them 1 to 2 weeks before surgery because of potential for perioperative complications but consult with the prescribing clinician.

**Ribavirin.** Ribavirin is an oral RNA nucleoside inhibitor and inhibits RNA functions required for viral replication. The drug is used in conjunction with pegylated interferons or other oral antivirals for the

treatment of HCV infection, including coinfection with HIV and HBV. Ribavirin has multiple potentially serious adverse effects, including anemia and cardiovascular disease (hypertension and myocardial infarction). No evidence-based guidelines or literature are available for perioperative management. Because most adverse effects are chronic, it is reasonable to continue ribavirin up to the day of surgery, but it should be held on the morning of surgery because of the need to take it with food.

*Consensus Recommendations:* Continue ribavirin up to the day of surgery but hold on the morning of surgery. If hemoglobin level has not recently been obtained, check it before surgery.

**Other Oral Anti-HCV Medications.** Several other oral anti-HCV medications have greater efficacy in achieving sustained virologic response and are used much more frequently than the aforementioned drugs. These include sofosbuvir, ledipasvir/sofosbuvir, sofosbuvir/valpatasvir, glecaprevir/pibrentasvir, dasabuvir/ombitasvir/paritaprevir/ritonavir, elbasvir/grazoprevir, and sofosbuvir/velpatasvir/voxilaprevir. Except for ritonavir, all these medications and their component drugs interfere with HCV viral RNA replication. Ritonavir is an HIV antiviral with no direct activity against HCV but is part of a combination with paritaprevir because it is a pharmacokinetic enhancer of that drug.

These medications are much better tolerated than interferons but still have important considerations. Sofosbuvir has several significant drug interactions, including amiodarone, PPIs, HIV antivirals, anticonvulsants, and antimycobacterials. Because of their cytochrome P450 metabolism, the other drugs in this group also have potential drug interactions with common perioperative medications. Elbasvir/grazoprevir, in particular, has several critical drug interactions, including opioids, antibiotics, benzodiazepines, and antiemetics. Glecaprevir/pibrentasvir, dasabuvir/ombitasvir/paritaprevir/ritonavir, and sofosbuvir/velpatasvir/voxilaprevir must also be taken with food. Data on the safety of these drugs in the perioperative setting are minimal, and

management recommendations are based on the adverse effects, drug interactions, and administration requirements.

*Consensus Recommendations:* Continue sofosbuvir and ledipasvir/sofosbuvir up to and including the day of surgery. Continue sofosbuvir/valpatasvir, glecaprevir/pibrentasvir, dasabuvir/ombitasvir/paritaprevir/ritonavir, elbasvir/grazoprevir, and sofosbuvir/velpatasvir/voxilaprevir up to the day of surgery but hold on the morning of surgery. Discuss management with the patient's gastroenterology clinician.

### **Gallstone Solubilizing Agents**

Ursodiol and chenodeoxycholic acid reduce gallstone formation after bariatric surgery and improve cholestasis in primary sclerosing cholangitis. No substantial perioperative literature is available for this class of medications, but when taken without food, they may cause nausea. For this reason and because their benefits are derived from long-term rather than short-term administration, withholding these medications while fasting is reasonable.

*Consensus Recommendation:* Continue gallstone solubilizing agents up to the day before surgery but hold on the morning of surgery.

### **Pancreatic Enzymes**

These agents are commonly used for patients with pancreatic insufficiency related to inflammation, trauma, or surgical resection. Essentially no data are available on perioperative management of these medications. They are considered safe perioperatively, although during preoperative fasting, they should be held because they are usually not necessary in this situation.

*Consensus Recommendation:* Continue pancreatic enzymes up to the day before surgery but hold on the morning of surgery.

### **5-Aminosalicylic Acid**

Drugs in the 5-aminosalicylic acid class are used to treat inflammatory bowel disease (IBD). Many clinicians have concerns about the potential for bleeding risk due to platelet inhibition, but these agents are considered

safe in the perioperative period because they have a primarily luminal impact with minimal systemic effects. A narrative review from 2011 recommended stopping 1 day in advance and resuming 3 days postoperatively in the setting of impaired glomerular filtration; however, in the setting of normal renal function, this is not necessary.<sup>33</sup> Adverse effects include hypersensitivity reactions, bone marrow suppression, pneumonitis, pancreatitis, and hemolytic anemia, but these are rare.

*Consensus Recommendations:* Continue 5-aminosalicylic acid medications up to and including the day of surgery but consider holding on the morning of surgery if glomerular filtration rate is below 50 mL/min.

### **Antidiarrheals**

Symptomatic management of diarrhea is accomplished by antimotility agents that work through either opioid receptor agonism or anticholinergic activity. Antidiarrheals are generally safe, although loperamide in excessive doses leads to euphoria, cardiotoxicity, and central nervous system and respiratory depression. Atropine has anticholinergic effects and may lead to anesthetic interactions, and a systematic review recommended loperamide and diphenoxylate/atropine conditionally in critically ill patients.<sup>34</sup> It is appropriate to continue these agents preoperatively up to the day before surgery because the quality of life benefit outweighs the perioperative risks, given the short half-life of these agents.

*Consensus Recommendations:* Continue antidiarrheals up to the day before surgery but hold on the morning of surgery because of the risk of opioid agonism and anticholinergic effects.

### **Anticholinergics and Antispasmodics**

Like antidiarrheal agents, these medications serve to slow gut transit time and reduce diarrhea, nausea, and vomiting as well as to control upper airway and gastric secretions. In the general setting, these medications have multiple adverse effects (tachyarrhythmias, hypertension, urinary retention, and altered mentation), and their use is discouraged in



elderly patients.<sup>10,35</sup> A recent analysis found the use of these agents to be associated with multiple adverse postoperative outcomes, including decreased survival and increased length of stay, readmission, and costs of care.<sup>36</sup> These medications have strong potential for contributing to perioperative neurocognitive dysfunction, and the American Society of Anesthesiologists' Brain Health Initiative recommends avoiding these agents in the surgical setting.<sup>37</sup>

*Consensus Recommendations:* Continue anticholinergics and antispasmodics up to the day before surgery but hold on the morning of surgery. Reexamine the long-term necessity of these medications (especially in elderly patients). Continuation of these agents is reasonable if it is absolutely needed for airway secretion control that could affect airway management.

### Lubiprostone

Lubiprostone is used to activate the chloride channel on the apical membrane of the gastrointestinal tract to increase intestinal fluid secretion and to improve fecal transit. This medication is used to treat opioid-related constipation and other causes of chronic constipation. There is a paucity of perioperative literature for this medication.

*Consensus Recommendation:* Continue lubiprostone up to and including the day of surgery.

### Guanylate Cyclase C Agonists

This medication class includes linaclotide and plecanatide and is used to treat chronic constipation by stimulating intestinal fluid secretion and transit. There is no significant perioperative literature for these medications, but they should be avoided in the setting of bowel obstruction or concerns for bowel perforation.

*Consensus Recommendation:* Continue guanylate cyclase C agonists up to and including the day of surgery.

### Peripheral Opioid Receptor Antagonists

SPAQI consensus recommendations for this class of medications have been published in a previous paper in this series, entitled

"Preoperative Management of Opioid and Nonopioid Analgesics: Society for Perioperative Assessment and Quality Improvement (SPAQI) Consensus Statement."<sup>2</sup>

### Serotonergic Neuroenteric Modulators

This class includes tegaserod, alosetron, and prucalopride; these agents are enteric 5-hydroxytryptamine receptor agonists that stimulate peristalsis and intestinal secretions. These agents typically do not manifest systemic serotonergic activity as their action is primarily luminal.<sup>38</sup> Preoperative administration of prucalopride has been reported to reduce intestinal inflammation and to shorten the duration of postoperative ileus.<sup>39</sup>

*Consensus Recommendation:* Continue serotonergic neuroenteric modulators up to and including the day of surgery.

### Laxatives

Laxatives, including bisacodyl, docusate, senna, and polyethylene glycol, may have multiple different mechanisms of action, but their primary goal is to help facilitate bowel movements in patients with constipation. There is no specific preoperative contraindication to the use of laxatives. However, clinicians may wish to avoid defecation risk in the operating room and the risk for gut motility disruption, especially before bowel surgery.

*Consensus Recommendation:* Continue laxatives up to the day before surgery but hold on the morning of surgery.

### Immunomodulators

This broad category of agents is used for autoimmune diseases of the gastrointestinal tract, such as IBD, or for transplant-related immunosuppression. One must balance the risks of organ rejection or recrudescence of autoimmune disease with the risk of impaired wound healing and infection risk. Published literature on the perioperative management of these medications is conflicting and includes only small single-center studies.

*Consensus Recommendations:* For patients taking these agents to prevent solid organ transplant rejection, continue up to and

including the day of surgery. For other indications, management must be individualized on the basis of patient and surgical factors, and the risks and benefits of continuation must be discussed with the surgeon and prescribing clinician (Table 3).

**Purine Analogues.** 6-Mercaptopurine and azathioprine have not been found to significantly increase the risk of postoperative complications.<sup>40</sup> For patients undergoing arthroplasty, American College of Rheumatology/American Association of Hip and Knee Surgeons (ACR/AAHKS) guidelines recommend continuing azathioprine uninterrupted through surgery for patients with severe systemic lupus erythematosus.<sup>41</sup>

*Consensus Recommendations:* Continue purine analogues up to and including the day of surgery but consult with the surgeon and prescribing clinician.

**Methotrexate.** Methotrexate may be used in the treatment of IBD and other autoimmune conditions. Similar to the purine analogues, studies to date have not identified an association between preoperative methotrexate use and increased perioperative complications.<sup>40,41</sup>

*Consensus Recommendations:* Continue methotrexate up to and including the day of surgery but consult with the surgeon and prescribing clinician.

**Tumor Necrosis Factor Inhibitors.** These agents inhibit tumor necrosis factor (TNF)-induced inflammatory processes and are used for IBD and other rheumatologic conditions. Use of TNF inhibitors increases the risk of infection as well as of certain malignant neoplasms. However, interruption of therapy can also result in loss of efficacy due to antibody development. Published studies of their perioperative use have been highly heterogeneous and yielded conflicting results, but most data do not suggest an increased risk of postoperative complications, except in combination with other immunomodulators.<sup>40,42</sup> Furthermore, the PUCINI trial's preliminary results also suggest that continuing these

agents does not increase infection risk.<sup>43</sup> However, until this study is published, it is problematic to advise routine perioperative continuation of these powerful immunosuppressants. In their guidelines for inflammatory arthritis and arthroplasty patients, the ACR/AAHKS advised not performing surgery for a full dosing cycle after the last administration.<sup>41</sup>

*Consensus Recommendation:* Withhold TNF inhibitors for at least 1 dosing interval before surgery (ie, if taken every 4 weeks, schedule surgery 5 weeks after the last dose) but consult with the surgeon and prescribing clinician to discuss the relevant risks and benefits of therapy interruption.

**Other Biologic Immunomodulators.** Ustekinumab, vedolizumab, and natalizumab are monoclonal antibodies used for the treatment of refractory IBD, but vedolizumab is unique for being gut specific. A retrospective single-center study with multivariate analysis of patients undergoing abdominal surgery found that increased postoperative infections were associated with biologic therapy only in combination with other immunosuppression.<sup>42</sup> In other studies, vedolizumab was not associated with increased risk for postoperative complications.<sup>44,45</sup> Other specific perioperative data are limited, but the ACR/AAHKS guidelines provide recommendations to withhold ustekinumab for 1 dosing cycle before surgery.<sup>41</sup>

Tofacitinib is a Janus kinase inhibitor used for the treatment of several autoimmune disorders, including ulcerative colitis that has failed to respond to treatment with TNF inhibitors. It is an oral medication with a much shorter half-life and is dosed twice daily. No specific literature has evaluated its safety in the surgical setting, but tofacitinib has a USFDA black box warning for increased risk of thrombosis that should be taken into consideration in the postoperative setting. The ACR/AAHKS guidelines recommend holding tofacitinib for 7 days before surgery.<sup>41</sup>

Ozanimod is a selective modulator of sphingosine 1-phosphate receptors originally

TABLE 3. Summary of Recommendations for the Preoperative Management of Gastrointestinal Immunomodulators

Medication class	Examples	Management before the morning of surgery	Management on the morning of surgery	Additional considerations
Purine analogues	6-Mercaptopurine, azathioprine	Continue	Continue	Consult with prescribing clinician and surgeon
Methotrexate		Continue	Continue	Consult with prescribing clinician and surgeon
Tofacitinib		Withhold for 7 days before surgery	Hold	Consult with the prescribing clinician and surgeon to discuss the relevant risks and benefits of therapy interruption
Ustekinumab		Withhold for at least 1 dosing interval before surgery <sup>a</sup>	Hold	Consult with the prescribing clinician and surgeon to discuss the relevant risks and benefits of therapy interruption
Natalizumab		Withhold for at least 1 dosing interval before surgery <sup>a</sup>	Hold	Consult with the prescribing clinician and surgeon to discuss the relevant risks and benefits of therapy interruption
Ozanimod		Withhold for at least 60 days before surgery	Hold	Consult with the prescribing clinician and surgeon to discuss the relevant risks and benefits of therapy interruption
Vedolizumab		Withhold for at least 1 dosing interval before surgery <sup>a</sup>	Hold	Consult with the prescribing clinician and surgeon to discuss the relevant risks and benefits of therapy interruption; perioperative continuation may be reasonable for nonabdominal surgery
Tumor necrosis factor inhibitors	Infliximab (and biosimilars), adalimumab (and biosimilars), golimumab and certolizumab	Withhold for at least 1 dosing interval before surgery <sup>a</sup>	Hold	Consult with the prescribing clinician and surgeon to discuss the relevant risks and benefits of therapy interruption

<sup>a</sup>That is, if taken every 4 weeks, schedule surgery 5 weeks after the last dose.

approved for treatment of multiple sclerosis but also approved in May 2021 as a once-daily oral medication for moderate to severe ulcerative colitis. Its therapeutic benefit is thought to be related to inhibited lymphocyte migration into the gastrointestinal tract, and use of ozanimod is associated with decreased blood lymphocyte counts. Ozanimod is also associated with increased risk of infections, bradyarrhythmias, and atrioventricular conduction delays, and its use with monoamine oxidase inhibitors is contraindicated because of potential for drug interactions. The mean half-life of active metabolites of ozanimod is approximately 11 days. No data on perioperative safety are available. On the basis of its immunosuppressant effects, we recommend discussion of perioperative management with the prescriber and surgeon and, if interruption of

therapy is pursued, holding of ozanimod for 5 half-lives to ensure adequate clearance before surgery.

**Consensus Recommendation:** Withhold vedolizumab, ustekinumab, and natalizumab for at least 1 dosing interval before surgery. Withhold ozanimod for 60 days and tofacitinib for 7 days before surgery but consult with the surgeon and prescribing clinician to discuss the relevant risks and benefits of therapy interruption. For vedolizumab, perioperative continuation may be reasonable for nonabdominal surgery.

### Weight Loss Medications

**Phentermine.** Phentermine is a sympathomimetic amine with pharmacologic properties similar to the amphetamines. The mechanism of action in reducing appetite appears to be secondary to central nervous

system effects, including stimulation of the hypothalamus to release norepinephrine. Available literature is somewhat variable, but most sources advise withholding before surgery because of the potential for cardiovascular adverse effects, the lack of evidence of serious withdrawal symptoms, and its use for a noncritical indication.<sup>46-48</sup>

**Consensus Recommendations:** Withhold phentermine for at least 4 days before surgery.

**Lisdexamfetamine.** This medication is used in patients with attention-deficit/hyperactivity disorder and binge eating disorder. It is a sympathomimetic amine that releases catecholamines from presynaptic nerve terminals and may block reuptake of catecholamines by competitive inhibition. Similar to phentermine, this medication has potential for cardiovascular adverse effects and is not associated with serious withdrawal symptoms. However, it has a shorter half-life than phentermine (12 hours vs 24 hours). There is an increased risk of serotonin syndrome when lisdexamfetamine is used concurrently with other serotonergic drugs, many of which are used perioperatively, including fentanyl and its metabolites and tramadol.

**Consensus Recommendations:** Withhold lisdexamfetamine for 72 hours before surgery if it is being taken for binge eating disorder. For patients at high risk for relapse of binge eating disorder, the medication may be continued before surgery and held only on the morning of surgery, but this requires discussion with the prescriber and anesthesiologist.

**Phentermine/Topiramate.** Phentermine is described earlier. Topiramate has appetite suppression and satiety enhancement by a variety of mechanisms, including blocking of neuronal voltage-dependent sodium channels, enhancement of  $\gamma$ -aminobutyric acid activity, antagonism of  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and kainite glutamate receptors, and weak inhibition of carbonic anhydrase. Topiramate has anticonvulsant activity, and withdrawal of phentermine/topiramate is associated with

increased risk for seizures as described in the product prescribing information.<sup>49</sup> Use of this medication combination can be associated with hypokalemia, hyperchloremic or non-anion gap metabolic acidosis, and increased creatinine concentration.

**Consensus Recommendations:** Withhold phentermine/topiramate for at least 4 days before surgery. Either wean the patient off the medication during the course of a week before surgery (according to product insert) or, while withholding, provide topiramate alone at the same dose.

**Orlistat.** This agent is a reversible inhibitor of gastric and pancreatic lipases that inhibits absorption of dietary fats. As a result, it exerts its effect with food ingestion and thus has little purpose in the preoperative fasting state. There are no other known adverse effects of perioperative concern.

**Consensus Recommendation:** Continue orlistat up to the day before surgery but hold on the morning of surgery.

**Liraglutide.** This treatment for type 2 diabetes mellitus is a long-acting analogue of glucagon-like peptide 1 (GLP-1) that slows gastric emptying and diminishes appetite. It is described in detail in a previously published article in this consensus statement series.<sup>3</sup>

**Consensus Recommendations:** Before the day of surgery, continue GLP-1 agonists unless there is heightened concern for postoperative nausea, vomiting, or gut dysfunction (eg, gastrointestinal surgery). In these situations, consider holding 24 hours for once- or twice-daily preparations and up to 1 week before surgery for weekly preparations (including holding dose within 7 days before surgery). Withhold GLP-1 agonists on the morning of surgery. If a weekly dose is due on the morning of surgery, delay taking it until later in the day after surgery.

**Bupropion/Naltrexone.** This preparation is a combination of an opioid antagonist and an inhibitor of dopamine and norepinephrine reuptake. The weight loss effects are not clearly understood but probably involve the hypothalamus and mesolimbic dopamine circuit.

No specific perioperative literature was identified on our review. Because of its blockade of opioid receptors, continuing the medication through procedures requiring opioids for postoperative analgesia is problematic.

**Consensus Recommendation:** Withhold bupropion/naltrexone for 72 hours before surgery if opioids are expected to be used perioperatively.

## CONCLUSION

Preoperative medication management is a crucial part of perioperative care. Evidence to guide practice in this area remains deficient, and clinical decision-making is predominantly determined through application of knowledge of medication mechanisms of action and adverse effects. Summarized in [Tables 1 to 3](#), this consensus statement provides recommendations of experts in anesthesiology, internal medicine, perioperative medicine, and medical subspecialties for the management of common pulmonary and gastrointestinal medications.

**Abbreviations and Acronyms:** **ACR/AAHKS**, American College of Rheumatology/American Association of Hip and Knee Surgeons; **COPD**, chronic obstructive pulmonary disease; **GLP-1**, glucagon-like peptide 1; **HBV**, hepatitis B virus; **HCV**, hepatitis C virus; **HIV**, human immunodeficiency virus; **5-HT**, 5-hydroxytryptamine; **IBD**, inflammatory bowel disease; **IPF**, idiopathic pulmonary fibrosis; **PDE**, phosphodiesterase; **PDE-5**, phosphodiesterase type 5; **PH**, pulmonary hypertension; **PPI**, proton pump inhibitor; **SPAQI**, Society for Perioperative Assessment and Quality Improvement; **TNF**, tumor necrosis factor; **USFDA**, US Food and Drug Administration

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