Guideline for the Perioperative Management of Biologic and Immunomodulatory Drugs for Inflammatory Conditions During Elective Surgery

Introduction

Biological and immunomodulatory medicines are used in the management of inflammatory conditions such as inflammatory bowel disease, inflammatory arthritis, psoriasis and multiple sclerosis. They modify the actions of the immune system which can drive inflammation and disease progression, but this can also affect pathways which protect against infections. As a result, some of these medicines need to be interrupted in the peri-operative period.

This guideline does not apply to patients receiving immunosuppressive drugs for organ transplantation.

Generic drug names have been used throughout

The potential prevention of post-operative infection by stopping biologics should be balanced against the risk of perioperative flare in disease activity. In many cases, a perioperative disease flare may lead to an increase in glucocorticoid dosing. This is associated with increased infection risk in a dose-dependent manner.

For most biologics, except where stated, surgery should be planned for when at least one dosing interval has elapsed for that drug. This is pragmatic advice as the nadir of the drug's effect would be at the end of its dosing interval; hence the immunosuppressant effects of the drug will be at its lowest.

Some medicines do not need to be stopped during the perioperative period. This is either because there is no evidence that these medicines cause harm in the perioperative period, because they are not considered especially immunosuppressive, or the condition being treated is unsuitable for the cessation of medication during the peri-operative period (multiple sclerosis for example).

Consider continuing biologics for low-risk procedures ((i.e. surgery without a break in sterile technique, during which the respiratory, gastrointestinal and genitourinary tracts are not entered) e.g. endoscopy, bronchoscopy, hysteroscopy, cystoscopy, breast biopsy, dermatologic or ophthalmological procedures).

In a minority of cases, the surgical team may deem the procedure to be of especially high infection risk. In this case, consider stopping the biologic for 5 half-lives prior to surgery to allow time to "wash-out" the biologic. Washout times are considered to be between 3 and 5 half-lives and there is significant inter-patient variation. For ease, only 5 half-lives have been included here, but this is a cautious approach. Consideration must be given to the risk of flare of the inflammatory condition when stopping drugs for this prolonged period as well as the risk of losing response to biologic therapies long-term. As a result, these situations must be discussed with the clinicians treating the inflammatory condition as well as the patient in order to weigh up the risks and benefits of this approach.

Recommence biologics post-operatively when there is good wound healing (typically around 14 days post-operatively), all sutures and staples are out, and there is no evidence of local or systemic infection. For JAK inhibitors (abrocitinib, baricitinib, filgotinib, tofacitinib and upadacitinib), aim to restart treatment 3-5 days post operatively to reduce the risk of relapse. Ideally treatment interruption should not exceed 14 days. Note that some drugs where indicated may require dose re-titration if stopping for prolonged periods – consult the specialist teams in these instances.

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Table 1: Biologic and Immunomodulatory medicines which do not usually require cessation during the perioperative period (but may be stopped if there are concerns – see notes):

Key	
Dermatology	
Rheumatology	
Neurology	
Gastroenterology	
Respiratory	

Drug	Notes
Azathioprine (multi-specialty)	Usually continue but stop T-14 days prior to surgery if procedure considered high risk in an individual patient
Ciclosporin (multi-specialty)	Usually continue but stop for T-14 days prior to surgery if procedure considered high risk in an individual patient
Dimethyl fumarate (Dermatology and Neurology)	Continue
Diroximel fumarate	Continue
Dupilumab (Dermatology and Respiratory)	Continue, not considered immunosuppressive
Eculizumab	Continue
Fingolimod	Continue due to risk of rebound
Glatiramer	Continue
Hydroxychloroquine	Continue
Interferon beta	Continue
Lebrikizumab	Continue, not considered immunosuppressive
Leflunomide	Usually continue due to long half-life (2 weeks). Will need washout procedure if wish to stop perioperatively – refer to SPC
Methotrexate (multi-specialty)	Usually continue but stop T-14 days prior to surgery if procedure considered high risk in an individual patient
6-Mercaptopurine (multi-specialty)	Usually continue but stop for T-14 days prior to surgery if procedure considered high risk in an individual patient
Mycophenolate mofetil	Continue
Nemolizumab	Continue, not considered immunosuppressive
Omalizumab (Dermatology and Respiratory)	Continue, not considered immunosuppressive
Ponesimod	Continue due to risk of rebound (missed doses may also require dose re-titration)
Siponimod fumaric acid	Continue due to risk of rebound (missed doses may also require dose re-titration)
Sulphasalazine	Continue

Teriflunomide	Usually continue due to long half-life (3 weeks). Will need washout procedure if wish to stop perioperatively – refer to Summary of Product Characteristics https://www.medicines.org.uk/emc
Tralokinumab	Continue, not considered immunosuppressive

Table 2: Biologic and Immunomodulatory medicines which do require caution or cessation during the peri-operative period:

Drug	When to schedule surgery relative to dosing interval	Timing of last dose if want to wash out for 5 half-lives
Abatacept	Schedule surgery to miss ONE dose i.e. last dose T-8 days prior to surgery (if on SC dose) or last dose T-29 days prior to surgery (if on IV dose)	T-70 days
Abrocitinib	Schedule surgery to miss TWO doses i.e. last dose on T-2 days prior to surgery	N/A
Adalimumab (multispecialty)	Schedule surgery to miss ONE dose – i.e. last dose on T-8 days prior to surgery (if on weekly dosing) or last dose T-15 days prior to surgery (if on fortnightly dosing). Consider continuing perioperatively if the patient is having IBD surgery	T-70 days
Apremilast (Rheumatology and Dermatology)	Schedule surgery to miss TWO doses i.e. last dose on T-2 days prior to surgery	N/A
Baricitinib (Rheumatology and Dermatology)	Schedule surgery to miss THREE doses i.e. last dose on T-3 days prior to surgery	N/A
Benralizumab	Schedule surgery to miss ONE dose i.e. last dose T-57 days prior to surgery (if on 8 weekly dosing)	T-77 days
Bimekizumab (Rheumatology and Dermatology)	Schedule surgery to miss ONE dose i.e. last dose T-29 days prior to surgery (if on 4 weekly dosing) or T-57 days prior to surgery (if on 8 weekly dosing)	T-112 days
Brodalumab	Schedule surgery to miss ONE dose i.e. last dose T-15 days prior to surgery (if on fortnightly dosing)	T-49 days
Certolizumab pegol (Rheumatology and Dermatology)	Schedule surgery to miss ONE dose i.e. last dose T-15 days prior to surgery (if on fortnightly dosing) or last dose T-29 days prior to surgery (if on 4 weekly dosing)	T-70 days
Cladribine	Schedule surgery at least TWO months after last dose i.e. T-57 days prior to surgery	N/A
Deucravacitinib	Schedule surgery to miss THREE doses i.e. last dose T-3 days prior to surgery	N/A
Etanercept	Schedule surgery to miss ONE dose i.e. last dose on T-5 days prior to surgery (if on twice weekly dosing) or last dose T-8 days prior to surgery (if on weekly dosing)	T-15 days
Etrasimod	Schedule surgery to miss SIX doses i.e. last dose T-6 days prior to surgery	N/A
Filgotinib (Rheumatology and Gastroenterology)	Schedule surgery to miss THREE doses i.e. last dose T-3 days prior to surgery	N/A
Golimumab (Rheumatology and Gastroenterology)	Schedule surgery to miss ONE dose i.e. last dose T-29 days prior to surgery (if on 4 weekly dosing). Consider continuing perioperatively if the patient is having IBD surgery	T-60 days

Guselkumab (multi-specialty)	Schedule surgery to miss ONE dose i.e. last dose T-57 days prior to surgery (if on 8 weekly dosing). Consider continuing perioperatively if the patient is having IBD surgery	T-84 days
Infliximab (multi-specialty)	Schedule surgery to miss ONE dose i.e. last dose T-15 days prior to surgery (if on SC dosing) or last dose T- 29 days prior to surgery (if on 4 weekly IV dosing), T-43 days prior to surgery (if on 6 weekly IV dosing), T- 57 days prior to surgery (if on 8 weekly IV dosing). Consider continuing perioperatively if the patient is having IBD surgery	T-196 days if IV T-56 days if SC
Ixekizumab (Rheumatology and Dermatology)	Schedule surgery to miss ONE dose i.e. last dose T-29 days prior to surgery (if on 4 weekly dosing)	T-63 days
Mepolizumab	Schedule surgery to miss ONE dose i.e. last dose T-29 days prior to surgery (if on 4 weekly dosing)	T-112 days
Mirikizumab	Schedule surgery to miss ONE dose i.e. last dose T-29 days prior to surgery Consider continuing perioperatively if the patient is having IBD surgery	T-49 days
Natalizumab	Schedule surgery for 1 week after last dose i.e. last dose T-8 days prior to surgery – note high risk of rebound if stopped	N/A
Ocrelizumab	Last dose between T-84 days and T-168 days prior to surgery	N/A
Ofatumumab	Schedule surgery for the end of the dosage interval, i.e. last dose T-27 days prior to surgery (if on 4 weekly dosing)	N/A
Ozanimod	Schedule surgery to miss FIVE doses i.e. last dose T-5 days prior to surgery (note will need re-titration to restart)	N/A
Risankizumab (multi-specialty)	Schedule surgery to miss ONE dose i.e. last dose T-57 days prior to surgery (if on 8 weekly dosing) or T-85 days prior to surgery (if on 12 weekly dosing). Consider continuing perioperatively if the patient is having IBD surgery	140 days
Ritlecitinib	Schedule surgery to miss TWO doses i.e. last dose T-2 days prior to surgery	N/A
Rituximab (Rheumatology and Dermatology)	Last dose between T-84 days and T-168 days prior to surgery	105 days
Sarilumab	Schedule surgery to miss ONE dose i.e. last dose T-15 days prior to surgery (if on fortnightly dosing)	T-105 days
Secukinumab (Rheumatology and Dermatology)	Schedule surgery to miss ONE dose i.e. last dose T-15 days prior to surgery (if on fortnightly dosing) or T-29 days prior to surgery (if on 4 weekly dosing)	T-133 days
Tildrakizumab	Schedule surgery to miss ONE dose i.e. last dose T- 85 days prior to surgery	T-119 days
Tocilizumab	Schedule surgery to miss ONE dose i.e. last dose T-15 days prior to surgery (if on SC dosing) or last dose T-29 days prior to surgery (if on IV dosing)	T-60 days for SC dosing T-90 days for IV dosing
Tofacitinib (Rheumatology and Gastroenterology)	Schedule surgery to miss THREE doses i.e. last dose T-3 days prior to surgery	N/A
Ublituximab	Last dose between T-84 days and T-168 days prior to surgery	N/A
Upadacitinib (multi-specialty)	Schedule surgery to miss THREE doses i.e. last dose T-3 days prior to surgery	N/A

Ustekinumab (multi-specialty)	Schedule surgery to miss ONE dose i.e. last dose T-57 days prior to surgery (if on 8 weekly dosing) or last dose T-85 days prior to surgery (if on 12 weekly dosing). Consider continuing perioperatively if the patient is having IBD surgery	T-105 days
Vedolizumab	Schedule surgery to MISS ONE dose i.e. last dose T-15 days prior to surgery (if on SC dosing), last dose T-29 days prior to surgery (if on 4 weekly IV dosing) or T-57 days prior to surgery (if on 8 weekly IV dosing). Consider continuing perioperatively if patient is having IBD surgery.	T-133 days

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