

Joint Guidelines for the Management of Interruption of Biologic Therapies for Elective Surgery in Adults and Children with Rheumatoid Arthritis, Psoriatic Arthritis, JIA and Ankylosing Spondylitis
 (see Gastroenterology and Dermatology guidelines for their patients)

For Use in:	Organisation-wide elective surgery preparation in patients receiving biologic drugs
By:	All clinicians and surgical pre-assessment staff involved in preparing patients for elective surgery
For:	Adults and Children with Rheumatological conditions requiring Biologic Therapy, who are undergoing elective surgical procedures
Division responsible for document:	Medical Division (Including Emergency)
Key words:	Biologics, Anti-TNF, Biosimilars, Rheumatoid Arthritis, arthritis, delayed healing, immunosuppression, infection, JIA, Psoriatic Arthritis, juvenile, risk
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Compliance links: (is there any NICE related to guidance)	No

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If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A
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Therapies Discussed in this Guideline including at the time of publication (others may be available in the future)

Class/Target	Trade Name	Generic Name	Biosimilar Name
Anti-TNF	Enbrel	Etanercept	Benepali, Erelzi
	Humira	Adalimumab	Amgevita, Imraldi
	Remicade	Infliximab	Remsima, Inflectra
	Cimzia	Certolizumab	
	Simponi	Golimumab	
B-cell Depletor	Mabthera	Rituximab	Rixathon, Truxima
IL 6	Roactemra	Tocilizumab	
	Sarilumab	Kevzara	
IL 17	Cosentyx	Secukinumab	
	Taltz	Ixekizumab	
T-cell Depletor	Orencia	Abatacept	
IL 12 / IL 13	Stelara	Ustekinumab	
JAK Inhibitor	Olumiant Xeljanz	Baracitinib Tofacitinib	
Immune Modulator	Otezla	Apremilast	

Quick reference Table

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For the purpose of this table, we are using generic names only

Drug	Dosing Interval	Period in which surgery should be scheduled (relative to last biologic dose administered)
Etanercept	Weekly or twice weekly	Week 2
Adalimumab	Every 2 weeks	Week 3
Infliximab	Every 4,6 or 8 weeks	Week 5,7 or 9
Certolizumab	Every 2 weeks	Week 3
Golimumab	Every 4 weeks	Week 5
Rituximab	Two doses 2 weeks apart, no more frequent than every 6 months	Months 4-7
Tocilizumab i.v.	Every 4 weeks	Week 5
Tocilizumab s.c.	Every week	Week 3
Sarilumab	Every 2 weeks	Week 4
Secukinumab	Monthly s/c	12 weeks
Ixekizumab	Monthly s/c	Week 10
Abatacept i.v	Monthly i.v.	Week 5
Abatacept s.c.	Weekly s.c.	Week 2
Ustekinumab	Every 12 weeks	Week 13
Baracitinib	Daily oral dose	Stop dosing 2 days prior to surgery
Tofacitinib	Twice daily oral dose	Stop dosing 2 days prior to surgery
Apremilast	Daily oral dose	Stop dosing 2 days prior to surgery

Recommence Biologics once Surgeon is happy with the wound and no other signs of infection, e.g. on antibiotics

Objective

Joint Guidelines for the Management of Interruption of Biologic Therapies for Elective Surgery in Adults and Children with Rheumatoid Arthritis, Psoriatic Arthritis, JIA and Ankylosing Spondylitis

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To enhance patient safety peri-operatively in terms of reducing risk of infection and promoting optimal wound healing

Rationale

Biologic Therapies are now widely used for the treatment Rheumatological conditions including rheumatoid arthritis, psoriatic arthritis, JIA and ankylosing spondylitis

Patients with rheumatological diseases have unique surgical risk factors, such as the exposure to disease modifying anti-rheumatic drugs (DMARDs) and corticosteroids that, in addition to their underlying disease, could predispose them to infections.

Tumour Necrosis Factor (TNF) mediates inflammation and modulates cellular immune responses. TNF inhibitors may therefore affect host defences against infection. This is thought to pose a risk for the development of postoperative infections and healing complications in patients with rheumatological diseases undergoing surgery.

The British Society of Rheumatology's (BSR) 2018 statement on the safety of biologic therapies encourages consideration of the risks and benefits of pausing biologics peri-operatively. (1)

Staff involved in preparing patients for elective surgery need to be aware of the rationale for pausing biologic therapy for Rheumatology patients and the specific time scales involved for each therapy. For concerns regarding individual cases, please contact the patient's rheumatology consultant for advice.

New patients starting on biologic therapies in the Rheumatology Department are given in depth counselling about the risks of infection generally and how to manage their therapy in the event of elective surgery.

Rheumatology biologics patients have a PAS alert to help identify that they are taking biologic therapies and the need to stop these agents prior to elective surgery. Patients are also given an alert card to remind them to stop their therapies prior to surgery. None of these mechanisms is failsafe however.

Broad recommendations

BSR guidance suggests that for most biologics, allow one dosing interval to elapse prior to surgery.

For higher risk procedures, consideration should be given to stopping **3 - 5 x half-lives** for the relevant drug before surgery.

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Biologic therapy should not be restarted after surgery until there is good wound healing (typically around 14 days), all sutures and staples are out, no evidence of infection, however subtle (2), and the surgeon is happy with the wound.

For **clean surgical procedures**, (i.e. arthroscopy) washout = **3 x half life**

For **high infection risk procedures**, (i.e. GI tract surgery) washout = **5 x half life**

Stop biologics prior to dental extractions

Stop biologics prior to biopsies resulting in open granulation tissue

Do not stop biologics prior to endoscopy, cystoscopy, liver/kidney biopsy, lymph node biopsy or punch biopsy

For bloodless procedures (such as cataract surgery) we would not advise routinely stopping biologics.

Note: Patients may flare when their biologic drug is stopped, and surgical outcomes may be adversely affected in a patient with systemic disease. If steroids are used to suppress flares whilst withholding the biologic drug, they may have an even greater adverse effect on surgical outcomes. Please contact the patient's Rheumatology consultant or the Biologics Specialist Nurses (x3786) for advice.

Advice regarding stopping DMARDS (ie Methotrexate) prior to Elective Surgery

We do not advocate stopping traditional DMARDS (methotrexate, leflunomide, sulphasalazine, hydroxychloroquine, ciclosporin, mycophenolate mofetil) peri-operatively. However if you have specific concerns about individual cases, please contact the patient's Rheumatology consultant.

Scope

The advice given in this guideline extends to the use of biosimilar biologic products. It also covers JAK inhibitors (ie Baracitinib) and Apremilast (immune modulator) which are not biologics, but are new agents. Our experience of using them is limited and we need further information regarding their risks in relation to elective surgery. Therefore, for safety reasons, we are currently recommending stopping these agents prior to surgery pending further safety data.

Clinical audit standards

To ensure that this document is compliant with the above standards, the following monitoring processes will be undertaken:

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Clinical audit will be carried out at a regular interval.
The aim of the audit is to ensure that:

‘All patients currently treated on biologics have appropriate interruption in treatment when undergoing surgery’

The audit will require information to be collected on:

- Which biologic treatment patient is taking
- Details of type of surgery
- Outcomes of the surgery, i.e. any post-operative infection
- Details of interruption in biologic treatment, i.e. stop and start dates

This audit may require use of patient electronic letters, medical notes and patient questionnaires. Results of audits will be shared with the Clinical Director and presented and discussed at Clinical Governance meetings.

Summary of development and consultation process undertaken before registration and dissemination

The authors listed above reviewed this guideline on behalf of the MDT in the Rheumatology Department across 3 Trusts, who have agreed the final content.

During its development it was / has been circulated for comment to:

Nurse Specialists, QEHLK
Rheumatology Consultants
Rheumatology Registrars
Rheumatology Specialist Nurses
Dr Joegi Thomas, Consultant Rheumatologist JPUH
Colin Green Pharmacist
Dr Anna Lipp, Consultant Anaesthetist
Pre-op Assessment Nurses
Orthopaedic surgeon
General surgeon
Plastics surgeon
Paediatric Rheumatology team

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