

**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)

<b>For Use in:</b>	Organisation-wide elective surgery preparation in patients receiving biologic drugs
<b>By:</b>	All clinicians and surgical pre-assessment staff involved in preparing patients for elective surgery
<b>For:</b>	Adults and Children with Rheumatological conditions requiring Biologic Therapy, who are undergoing elective surgical procedures
<b>Division responsible for document:</b>	Medical Division (Including Emergency)
<b>Key words:</b>	Biologics, Anti-TNF, Biosimilars, Rheumatoid Arthritis, arthritis, delayed healing, immunosuppression, infection, JIA, Psoriatic Arthritis, juvenile, risk
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<b>Assessed and approved by the:</b>	Clinical Guidelines Assessment Panel (CGAP) Chair's Action; tick here ✓
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<b>Ratified by or reported as approved to (if applicable):</b>	Clinical Safety and Effectiveness Sub-Board
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<b>To be reviewed by:</b>	Nicola Kerrigan
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<b>Version No:</b>	5
<b>Description of changes:</b>	QEH header added – document now a 3 Trust guideline
<b>Compliance links: (is there any NICE related to guidance)</b>	No

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

<b>Class/Target</b>	<b>Trade Name</b>	<b>Generic Name</b>	<b>Biosimilar Name</b>
<b>Anti-TNF</b>	Enbrel	Etanercept	Benepali, Erelzi
	Humira	Adalimumab	Amgevita, Imraldi, Idacio
	Remicade	Infliximab	Remsima, Inflectra
	Cimzia	Certolizumab	
	Simponi	Golimumab	
<b>B-cell Depletor</b>	Mabthera	Rituximab	Rixathon, Truxima
<b>IL 6</b>	Roactemra	Tocilizumab	
	Sarilumab	Kevzara	
<b>IL 17</b>	Cosentyx	Secukinumab	
	Taltz	Ixekizumab	
<b>T-cell Depletor</b>	Orencia	Abatacept	
<b>IL 12 / IL 13</b>	Stelara	Ustekinumab	
<b>JAK Inhibitor</b>	Olumiant	Baracitinib	
	Xeljanz	Tofacitinib	
	Jyseleca	Filgotinib	
	Rinvoq	Upadacitinib	
<b>Immune Modulator</b>	Otezla	Apremilast	
<b>IL23</b>	Skyrizi	Risankizumab	
	Tremfya	Guselkumab	

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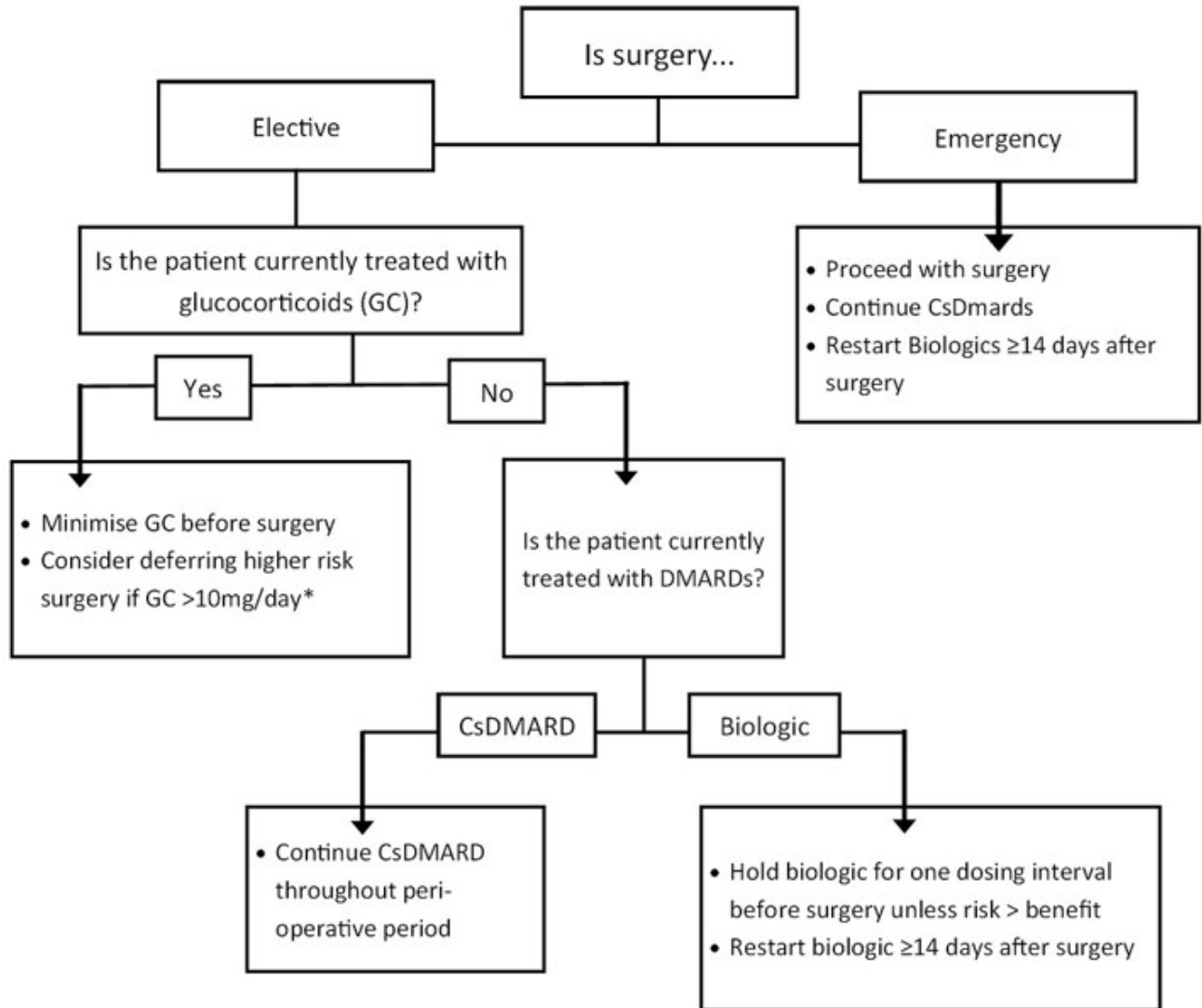
IL1-RA Interleukin-1 receptor antagonist	Kineret	Anakinra	
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**1. Quick reference Table**

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

<b>Drug</b>	<b>Dosing Interval</b>	<b>Period in which surgery should be scheduled (relative to last biologic dose administered)</b>
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
Guselkumab	4-8wkly s/c	Week 5-9
Risankizumab	Every 4 weeks s/c	Week 5
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
Filgotinib	Daily oral dose	Stop 2 days prior to surgery
Upadacitinib	Daily oral dose	Stop 2 days prior to surgery
Apremilast	Daily oral dose	Stop dosing 2 days prior to surgery

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**Suggested approach to patients with rheumatoid arthritis undergoing major surgery**

\* Surgeries with prosthetic material and abdominal surgeries are of particular concern

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***Resumption of Biologic therapies:*** *Biologics can be recommenced around 14 days post-operatively once the Surgeon is happy with the wound, the surgical site is healing well and there are no signs of local or systemic infection*

## **2. Objective**

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

## **3. 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 conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), Biologics (bDMARDs), 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.

## **4. Broad recommendations**

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

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

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, local or systemic, 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.

## **5. Advice regarding stopping DMARDS (ie Methotrexate) prior to Elective Surgery**

We do not advocate stopping conventional synthetic DMARDS(csDMARDS) (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.

## **6. 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.

## **7. Clinical audit standards**

# **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)**

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

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.

## **8. 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, QEHL  
Rheumatology Consultants  
Rheumatology Registrars  
Rheumatology Specialist Nurses  
Dr Joegi Thomas, Consultant Rheumatologist JPUH  
Pharmacist  
Dr Chris Sharpe Consultant Anaesthetist  
Pre-op Assessment Nurses  
Orthopaedic surgeon  
General surgeon  
Plastics surgeon  
Paediatric Rheumatology team  
Kings Lynn Rheumatology team

## **9. Glossary of common terms**



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<b>ACR</b>	American College of Rheumatology
<b>AS</b>	Ankylosing Spondyloarthritis or Axial Spondyloarthropathy
<b>bDMARDs</b>	Biologic Disease-Modifying Anti-Rheumatic Drugs. See <i>Biologics</i>
<b>Biologics</b>	Umbrella term for a class of drugs which use synthesised monoclonal antibodies to mediate inflammation caused by auto-immune diseases. See <i>Therapies discussed in this Guideline</i> for examples.
<b>Biosimilar</b>	Generic versions of a Biologic therapy. Identical to the originator. See <i>Originator</i>
<b>BSR</b>	British Society of Rheumatology
<b>csDMARDs</b>	Conventional Synthetic Disease-Modifying Anti-Rheumatic Drugs e.g. Methotrexate, Hydroxychloroquine, Azathioprine which are used as first-line immunosuppressive treatment for many Rheumatic conditions. There is no evidence to indicate csDMARDs should be stopped peri-operatively.
<b>Glucocorticosteroids</b>	Steroids, e.g. prednisolone, IM Depo-Medrone
<b>IA</b>	Inflammatory Arthritis
<b>JAKi</b>	Janus Kinase inhibitors. See <i>Therapies discussed in this Guideline</i> for examples.
<b>JIA</b>	Juvenile Inflammatory Arthritis
<b>Originator</b>	First marketed form of a Biologic therapy
<b>PsA</b>	Psoriatic Arthritis
<b>RA</b>	Rheumatoid Arthritis
<b>Tumour Necrosis Factor</b>	Immune system modulating protein targeted by Anti-TNF medication. See <i>Therapies discussed in this Guideline</i> for examples.

## 10. References

- 1 Holroyd C, et al The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis Rheumatology 2018 doi:10.1093 or via BSR website
- 2 Giles JT, Bartlett SJ, Gelber AC et al. Tumor necrosis factor inhibitor therapy and risk of serious postoperative orthopedic infection in rheumatoid arthritis. Arthritis Rheum 2006;55:333\_7.
- 3 SmPC for Secukinumab (Cosentyx) (Internet). Date of revision of text 23/10/2018 Available from [Novartis.customercare@novartis.com](mailto:Novartis.customercare@novartis.com)
- 4 SmPC for Ixekizumab (Taltz) [Internet] date of revision of text 24 May 2018. Available from [www.lilly.co.uk](http://www.lilly.co.uk)
- 5 SmPC for Baricitinib (Olumiant) (Internet) Date of revision of text 27/09/18 Available from [www.lilly.co.uk](http://www.lilly.co.uk)

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- 6 SmPC for Tofacitinib (Xeljanz) (Internet) Date of revision of text 11/2018  
Available from [www.pfizermedicalinformation.co.uk](http://www.pfizermedicalinformation.co.uk)
- 7 SmPC for Sarilumab (Kevzara) (Internet) Date of revision of text 24/08/2017  
Available from [uk-medicalinformation@sanofi.com](mailto:uk-medicalinformation@sanofi.com)
- 8 SmPC for Apremilast (Otezla) (Internet) Date of revision of text 19/12/2018  
Available from [medinfo.uk.ire@celgene.com](mailto:medinfo.uk.ire@celgene.com)
- 9 George M, Baker J, Perioperative management of immunosuppression in patients with rheumatoid arthritis Curr Opin Rheumatol. 2019 May; 31 (3): 300-306.