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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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If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

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(see Gastroenterology and Dermatology guidelines for their patients)

Therapies Discussed in this Guideline including at the time of publication (others may be available in the future)

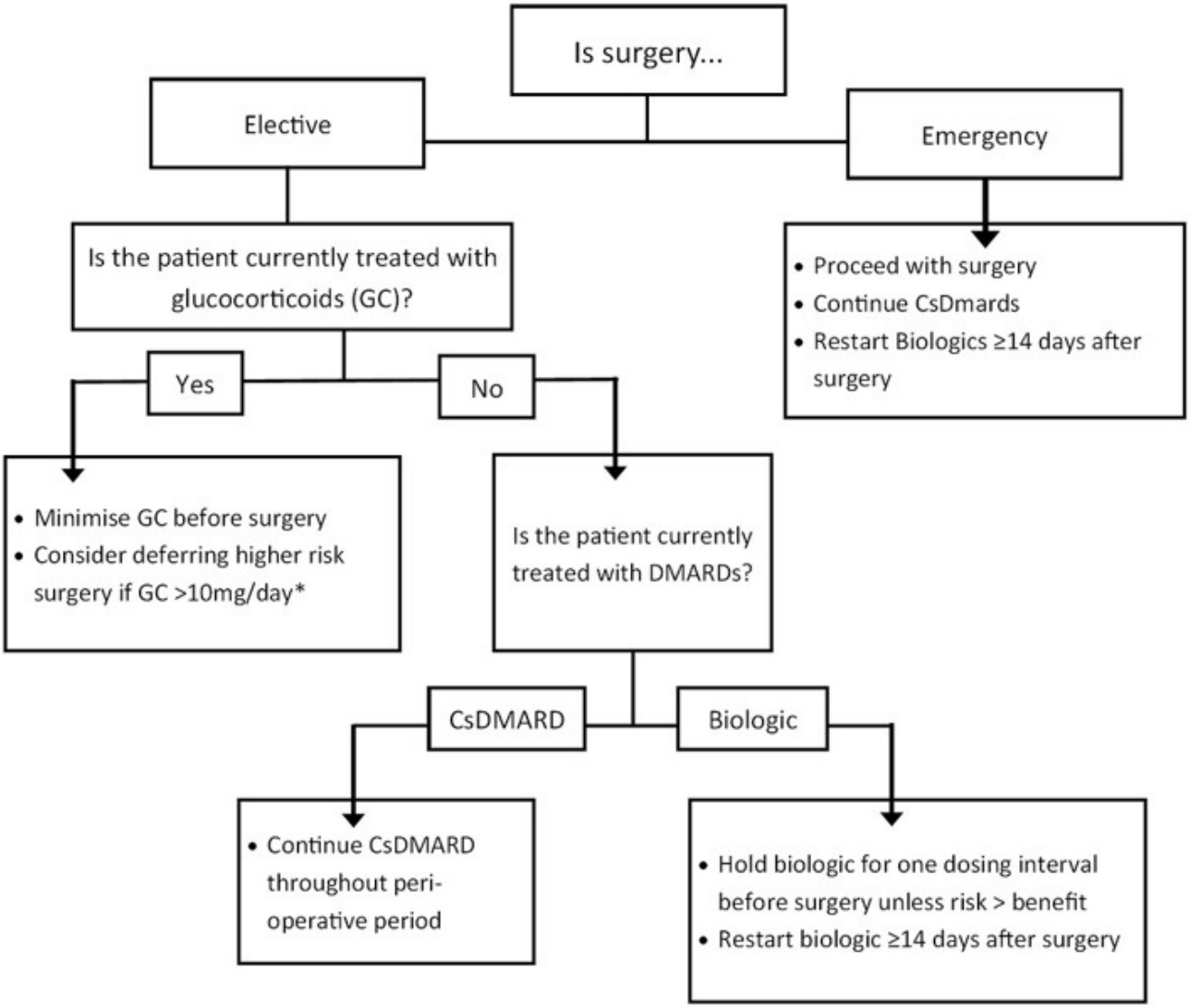
Class/Target	Trade Name	Generic Name	Biosimilar Name
Anti-TNF	Enbrel Humira Remicade Cimzia Simponi	Etanercept Adalimumab Infliximab Certolizumab Golimumab	Benepali, Erelzi Amgevita, Imraldi, Idacio Remsima, Inflectra
B-cell Depletor	Mabthera	Rituximab	Rixathon,Truxima
IL 6	Roactemra Sarilumab	Tocilizumab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

IL1-RA Interleukin-1 receptor antagonist	Kineret	Anakinra	

1. Quick reference Table

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. Tocilizumab s.c.	Every 4 weeks Every week	Week 5 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 Abatacept s.c.	Monthly i.v. Weekly s.c.	Week 5 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



Suggested approach to patients with rheumatoid arthritis undergoing major surgery

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

Recommencement 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.

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

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, QEHKL
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

ACR	American College of Rheumatology
AS	Ankylosing Spondyloarthritis or Axial Spondyloarthropathy
bDMARDs	Biologic Disease-Modifying Anti-Rheumatic Drugs. See *Biologics*
Biologics	Umbrella term for a class of drugs which use synthesised monoclonal antibodies to mediate inflammation caused by auto-immune diseases. See *Therapies discussed in this Guideline* for examples.
Biosimilar	Generic versions of a Biologic therapy. Identical to the originator. See *Originator*
BSR	British Society of Rheumatology
csDMARDs	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.
Glucorticosteroids	Steroids, e.g. prednisolone, IM Depo-Medrone
IA	Inflammatory Arthritis
JAKi	Janus Kinase inhibitors. See *Therapies discussed in this Guideline* for examples.
JIA	Juvenile Inflammatory Arthritis
Originator	First marketed form of a Biologic therapy
PsA	Psoriatic Arthritis
RA	Rheumatoid Arthritis
Tumour Necrosis Factor	Immune system modulating protein targeted by Anti-TNF medication. See *Therapies discussed in this Guideline* 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

4 SmPC for Ixekizumab (Taltz) [Internet] date of revision of text 24 May 2018. Available from www.lilly.co.uk

5 SmPC for Baricitinib (Olumiant) (Internet) Date of revision of text 27/09/18 Available from www.lilly.co.uk

6 SmPC for Tofacitinib (Xeljanz) (Internet) Date of revision of text 11/2018 Available from www.pfizermedicalinformation.co.uk

7 SmPC for Sarilumab (Kevzara) (Internet) Date of revision of text 24/08/2017 Available from 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

9 George M, Baker J, Perioperative management of immunosuppression in patients with rheumatoid arthritis Curr Opin Rheumatol. 2019 May; 31 (3): 300-306.