TREATMENT PATHWAY FOR THE MANAGEMENT OF ADULTS WITH MODERATE TO SEVERE PSORIATIC ARTHRITIS IN SECONDARY CARE.

(FOR SPECIALIST INITIATION ONLY)

TARGET AUDIENCE	All clinical staff working within Rheumatology in secondary care.
PATIENT GROUP	Adults with Moderate to Severe Psoriasis AND inadequate response to conventional synthetic disease-modifying antirheumatic drugs.

Clinical Guidelines Summary

- This guideline outlines the management pathway for adult patients with moderate to severe psoriasis who have three or more tender joints and three or more swollen joints, and who have had an inadequate response to, or have contraindications for, one or more standard systemic therapies, including methotrexate, sulfasalazine, and leflunomide.

- Treatment choices should be made following a discussion between the clinician and the patient about the advantages and disadvantages of the available treatments. This discussion should also consider associated conditions, such as extra-articular manifestations. Treatment should typically begin with the least expensive drug, considering administration costs, required dose, and product price per dose. However, individual variations in the method of administration and treatment schedules may necessitate adjustments for specific patients.

- The pathway provides a stepwise approach to the management of psoriatic arthritis with biologic or small molecule therapy.

Treatment Pathway for the Management of Adults with Psoriatic Arthritis following inadequate response to DMARDs.

NHS Lanarkshire

Active Psoriatic Arthritis (≥3 tender and ≥3 swollen joints) No-response to at least 2 DMARDS (individually or in combination)

First line therapy

1 st choice - Adalimumab, Infliximab, Etanercept, Golimumab, Certolizumab.

If anti-TNF contraindicated – Bimekizumab, Secukinumab, Ixekizumab, Apremilast, Tofacitinib, Upadicitinib

Drug with the lowest acquisition cost should be used first line, taking into account clinical and patient factors

Biologic response assessment - Adalimumab, Etanercept, Certolizumab, Golimumab, Infliximab, Tofacitinib, Upadicitinib– 12-14 weeks Bimekizumab, Secukinumab, Apremilast, – 16 weeks, Ixekizumab - 16-20 weeks.

Improvement in ≥2 of 4 PsARC criteria ≥1 to be tender or swollen joint. No worsening in any criteria If there is a PASI 75 response but the PsARC scored does not meet continuation criteria consider dermatologist assessment to determine whether continuation appropriate on the basis of skin response

Primary failure/Adverse reaction

If anti-TNF was used consider another agent with a different mode of action: Bimekizumab, Secukinumab, Ixekizumab, Ustekinumab, Tofacitinib, Upadicitinib, Apremilast

Positive responder

Continue therapy
Monitor with 6 monthly

If continued NICE response and stable, consider dose reduction

Secondary failure Initiate drug with a different mode of action to failed therapy

If 1st line was not an anti-TNF - Adalimumab, Etanercept, Infliximab, Certolizumab or Golimumab

If 1st line was an anti-TNF – initiate another anti-TNF, Bimekizumab, Secukinumab, Ixekizumab, Ustekinumab, Tofacitinib, Upadicitinib, Apremilast.

If anti-TNF is contraindicated – Bimekizumab, Secukinumab, Ixekizumab, Ustekinumab, Tofacitinib, Upadicitinib, Apremilast,

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Failed Response (Secondary Failure)
Patient can be initiated on another drug with a different mode of action to previous therapies.

* Nice TA 537 states that some patients with initial partial response may subsequently improve with continued treatment beyond 20 weeks

Psoriatic Arthritis Response Criteria (PsARC)

A PsARC response is defined as an improvement in at least two of the following measures, one of which must be the joint tenderness or swelling score, with no worsening in any of the four measures:

1.Patient global self-assessment (on a 1-5 Likert scale).

2.Physician global assessment (on a 1-5 Likert scale).

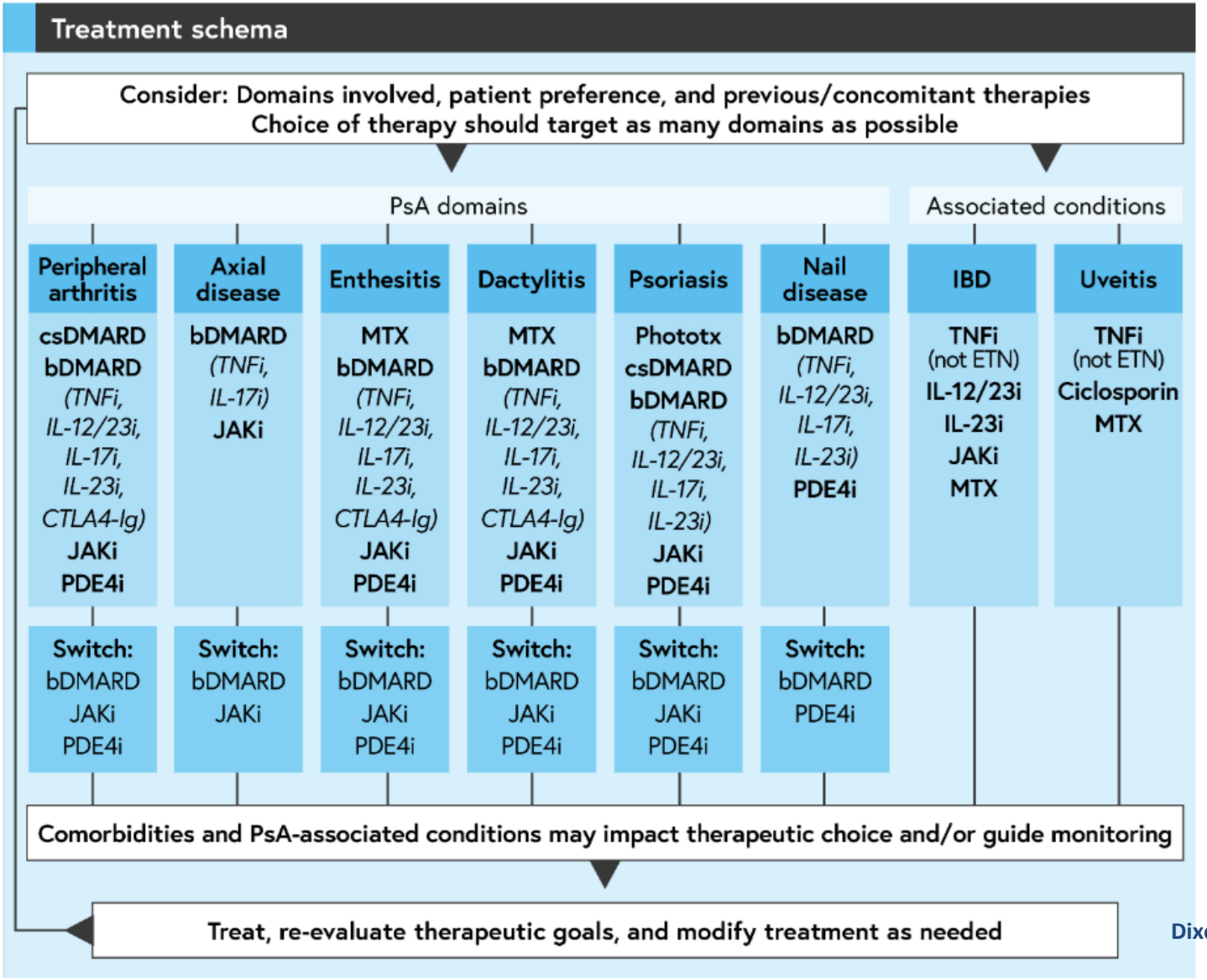
Improvement in scores 1 and 2 defined as decrease by at least 1 unit, and worsening defined as an increase by 1 unit.

3.Tender joint score (out of 68 joints).

4.Swollen joint count (out of 66 joints)

Improvement in scores 3 and 4 defined as decrease of at least 30% and worsening defined as an increase of at last 30%

Psoriatic arthritis management guidelines (GRAPPA)



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Current list of biologics/small molecules licensed for PsA

Mode of Action	SMC	Drug	First line	Initial review	Monotherapy	Offer (preferably) for patients with		
						Dactylitis	Enthesitis	Nail Changes
Anti-TNF	218/05	Adalimumab	Yes	12 weeks	✓	✓	✓	✓
	674/11	Golilumab	Yes	12 weeks	✓ or use with MTX	✓	✓	✓
	973/14	Certolizumab	Yes	12 weeks	✓ or use with MTX	✓	✓	✓
	107/04	Etanercept	Yes	12 weeks	✓	✓	✓	✓
		Infliximab	Yes	12 weeks	✓ or use with MTX	✓	✓	✓
PDE4inhibitor	1053/15	Apremilast	Yes	12 weeks	✓ or use with any cDMARD	✓	✓	✓

IL-17 inhibitor	2605	Bimekizumab	2 nd line	16 weeks	✓ or use with MTX	✓	✓	✓
	1167/16	Secukinumab	2 nd line	16 weeks	✓ or use with MTX	✓	✓	✓
	2097	Ixekizumab	2 nd line	16 weeks	✓ or use with MTX	✓	✓	✓
IL-23	2360	Guselkumab	3rd line	16 weeks	✓ or use with MTX	✓	✓	✓
	2459	Risankizumab	3rd line	16 weeks	✓ or use with MTX	✓	✓	✓
IL-12/23	944/14	Ustekinumab	3rd line	24 weeks	✓ or use with MTX	✓	✓	✓
JAK inhibitors	2116	Tofacitinib	2 nd line	12 weeks	Must use with MTX	✓	✓	✓

	2361	Upadacitinib	2 nd line	12 weeks	✓ or use with MTX	✓	✓	✓

Vaccinations:

- Annual flu/Covid vaccines recommended.
- Pneumococcal vaccination 2- 4 weeks before initiation. Only repeat after 5 years if asplenic/splenic dysfunction or Chronic Kidney Disease 4 or 5 (will also require Hep B vaccination).
- Check VZV serology prior to commencing and refer for vaccination if required.

Pre-screening Checks

- Complete pre-screening checklist with patient.
- Screen for TB, viral hepatitis, HIV and VZV serology prior to commencing biologic.
- Baseline U&Es, LFTs, FBC should be checked and then 6 monthly.
- CXR/BBV screen/QF Gold to be repeated if switching and >1 year since last screened.

Prescribing Notes:

Anti-TNFs:

- Avoid anti-TNF if demyelination disease/TB risk/moderate or severe heart failure.
- Certolizumab is the biologic of choice in pregnancy/breastfeeding/patient planning a pregnancy during treatment.
- Etanercept – not routinely recommended for psoriatic arthritis as less effective than the other biologics and should be avoided in patients with inflammatory eye disease and inflammatory bowel disease

IL-17 Inhibitors:

- Caution with IL-17 inhibitors in the presence of inflammatory bowel disease/recurrent candida.
- IL-17 inhibitors as a class are considered to have a relatively fast onset of action compared to other agents.

Phosphodiesterase inhibitors:

- A dose of 30mg once daily is recommended in patients with severe renal impairment (CrCl < 30mLmin). During dose titration, it is recommended using the AM scheduled dose only (the PM dose should be skipped)
- Suicidal thoughts and behaviour, including completed suicide, have been reported in patients with or without a history of depression
- Carefully assess the benefits and risks of starting or continuing treatment in patients with a history of psychiatric symptoms, or in those who are taking other medicines likely to cause psychiatric symptoms
- Patients should be instructed to report any changes in behaviour and treatment should be stopped if patients experience new psychiatric symptoms or if existing symptoms get worse.

Janus kinase (JAK) inhibitors:

- An increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality, was observed in patients treated with some JAK inhibitors, particularly tofacitinib, when compared to those treated with anti-TNFs.
- It is advised to avoid prescribing JAK inhibitors unless there are no suitable alternatives in patients with the following risk factors: age 65 or older, current, or past long-time smoking and other factors for cardiovascular disease or malignancy.
- Avoid in Pregnancy and breastfeeding.

A tool for approximate risk stratification in JAK inhibitor prescribing

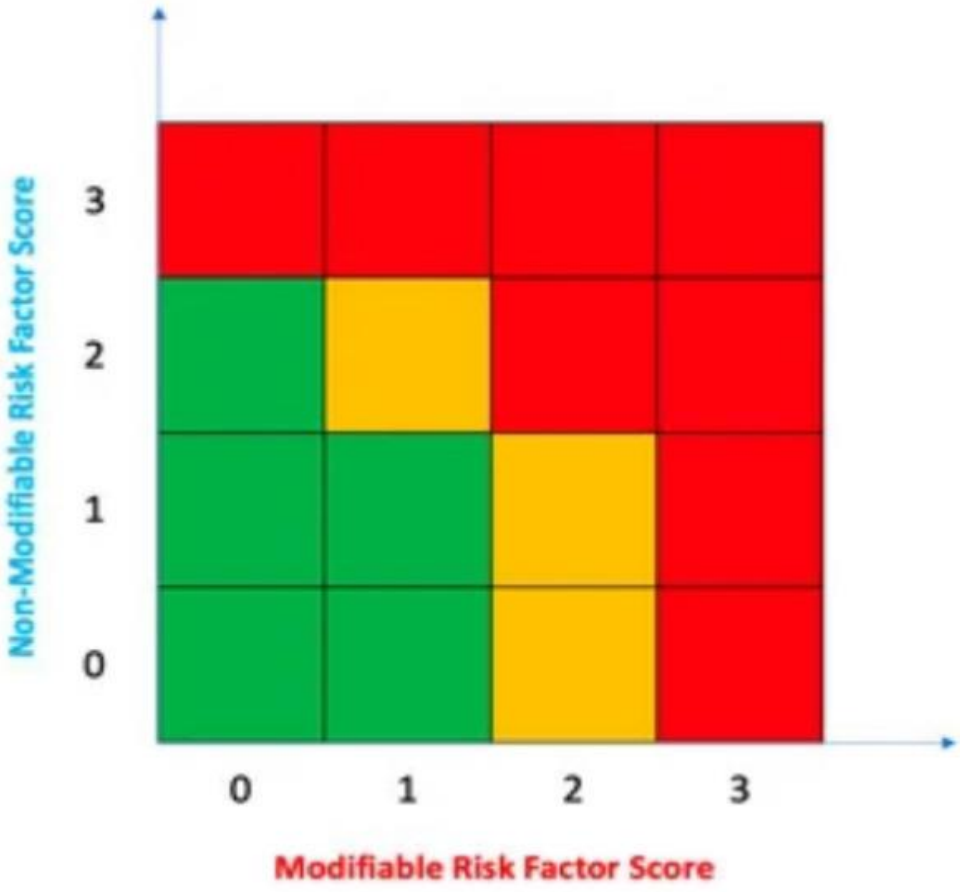
Non-Modifiable Risk Factors Scores:	
Age > 65	1
Male	1
Hx of MI, CVA, VTE	3
Hx of Malignancy	3

Add risk factors for total NMRF Score

Modifiable Risk Factors Scores:	
Poorly controlled HTN (BP > 140/90)	1
Poorly controlled DM (HbA1C > 75mmol/mol)	1
Poorly controlled Hyperlipdemia (LDL > 4nmol/L)	1
COCP	1
Smoking	2

Add risk factors for total MRF Score

- JAKi likely safe
- Risk-benefit may be acceptable in certain cases after discussion with patient
- JAKi not advised



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Transfer of Information to Primary Care:

Drug name (Biosimilar or equivalent) and dosing schedule must be documented in clinic letter, along with an ask of primary care to add to repeat prescription as a medication prescribed elsewhere. This allows the ECS to update.

Drug regimens

Drug	Target	**Adult Dosing regimen** (all SC administration unless stated otherwise)
Adalimumab	**Anti-TNF**	40mg – every 2 weeks
Aprelimast	**PDE4inhibitor**	Initially 10 mg daily on day 1, then 10 mg twice daily on day 2, then 10 mg in the morning and 20 mg in the evening on day 3, then 20 mg twice daily on day 4, then 20 mg in the morning and 30 mg in the evening on day 5, then maintenance 30 mg twice daily
Bimekizumab	**IL-17A/F**	PsA-160mg every 4 weeks PsA with Plaque Psoriasis: Loading: 320 mg - Week 0, 4, 8, 12, 16 Maintenance: 320mg – every 8 weeks. After 16 weeks clinical assessment is recommended and if a sufficient clinical response in joints cannot be maintained a switch to 160 mg every 4 weeks can be considered.
Certolizumab pegol	**Anti-TNF**	Loading: 400mg - Week 0, 2, 4 Maintenance: 200mg – every 2 weeks (Can be increased to 400mg if suboptimal response. Safe in pregnancy)
Golilumab	**Anti-TNF**	50 mg monthly. 100mg monthly, in patients >100 kg who do not achieve an adequate response on 50 mg monthly after 3-4 doses
Guselkumab	**IL-23**	Loading: 100mg - Week 0, 4 Maintenance: 100mg – every 8 weeks Option for 100mg every 4 weeks based on clinical judgement if considered high risk of joint damage.

Infliximab	**Anti-TNF**	Loading: Initially 5 mg/kg, then 5 mg/kg, to be taken at week 2 and 6 after initial dose. Maintenance:5 mg/kg every 8 weeks.
Ixekizumab	**IL-17**	For patients with concomitant moderate to severe plaque psoriasis, the recommended dosing regimen is the same as for plaque psoriasis: Loading: 160mg - Week 0 THEN 80mg – week 2, 4, 6, 8, 10, 12 Maintenance: 80mg – every 4 weeks OR 160mg at week 0 then 80mg every 4 weeks
Risankizumab	**IL-23**	Loading: 150mg - Week 0, 4 Maintenance: 150mg – every 12 weeks
Secukinumab	**IL-17**	Loading: 150mg or 300mg - Week 0, 1, 2, 3, 4 Maintenance: 150mg or 300mg – once per month
Tofacitinib	**JAK 1 and 3 inhibitor**	5mg BD
Ustekinumab	**IL -12/23**	Loading: 45mg - Week 0, 4 Maintenance: 45mg – every 12 weeks (If weight >100kg, increase dose to 90mg)
Upadicitinib	**JAK 1inhibitor**	15mg OD

Note: Biologics should be prescribed by Brand.

Abbreviations:

PASI – Psoriasis Area Severity Index, PsA – psoriatic arthritis

Peri-conception and pregnancy compatibility

Drug	Time to continue contraception after treatment cessation	Compatibility with trimesters [BSR 2022]		
		Peri- conception	First trimester	Second/ Third Trimester
Adalimumab	5 months	Yes	Yes	Yes
Apremilast	No advice	No studies identified in BSR guidance		
Certolizumab	5 months	Yes	Yes	Yes
Etanercept	3 weeks	Yes	Yes	Yes
Golimumab	6 months	Yes	Yes	Yes
Guselkumab	12 weeks	Not included in BSR guidance.		
Infliximab	6 months	Yes	Yes	Yes
Ixekizumab	10 weeks	Consider stopping at conception**	Severe disease if no alternatives**	Severe disease if no alternatives
Risankizumab	21 weeks	Not included in BSR guidance.		
Secukinumab	20 weeks	Consider stopping at conception**	Severe disease if no alternatives**	Severe disease if no alternatives
Tofacitinib*	4 weeks	Stop ≥2 weeks preconception	No	No
Upadacitinib*	4 weeks	Stop ≥2 weeks preconception	No	No

Ustekinumab	15 weeks	Consider stopping at conception**	Severe disease if no alternatives**	Severe disease if no alternatives

* However, as effects of JAK inhibitors may persist after drug elimination, a waiting period of one menstrual cycle before conception is advised.

** May be considered to manage severe maternal disease if no other pregnancy-compatible drugs are suitable.

Further information to support decision-making is available from:

- BSR guidance on prescribing of drugs in pregnancy and lactation
- Summaries of product characteristics (www.medicines.org.uk)
- UK Teratology Information Service (UKTIS) at https://uktis.org or 0344 892 0909 (Monday-Friday, 9am-5pm).

Exposures in pregnancy should be reported to UKTIS by use of their online reporting form (https://uktis.org/surveillance/reporting-an-exposure-in-pregnancy/). UKTIS are commissioned by the UK Health Security Agency (formerly Public Health England) to perform national surveillance of known and emerging human teratogens across the UK.

Advice and risk assessment for individual patients may also be available by contacting a local medicines information service via hospital pharmacy departments.

Vaccination of infants exposed to drugs due to maternal treatment

Immunisation schedules in infants after in-utero exposure to biologics will depend on timing of exposure, bioavailability and persistence of the drug, mechanism of action of the drug, and live vaccine. (20) The BSR recommend that:

• Women considered to have low risk of disease flare on withdrawal of anti-TNF in pregnancy could stop infliximab at 20 weeks, adalimumab and golimumab at 28 weeks and etanercept at 32 weeks so that a full-term infant may receive the normal UK vaccination schedule, including rotavirus vaccine at 8 weeks.

• Adalimumab, etanercept, infliximab or golimumab may be continued throughout pregnancy, to maintain disease control. In such case, immunisation with live vaccines should be avoided until infants are 6 months of age.

• Exposure to certolizumab in utero does not require any changes to vaccination schedule.

Pregnancy exposure and impact on infant live vaccines schedule

Drug	Pregnancy exposure and impact on infant live vaccines schedule
Adalimumab	If stopped by 28 weeks, full term infant can have a normal vaccination schedule. If used till term, avoid live vaccinations in infant vaccination schedule until 6 months of age.
Apremilast	No studies found in last BSR guidance update.
Certolizumab	No adjustment to vaccination including live vaccines needed.
Etanercept	If stopped by 32 weeks, full term infant can have a normal vaccination schedule. If used till term, avoid live vaccinations in infant vaccination schedule until 6 months of age.
Golimumab	If stopped by 28 weeks, full term infant can have a normal vaccination schedule. If used till term, avoid live vaccinations in infant vaccination schedule until 6 months of age.
Guselkumab	Not included in BSR guidance.
Infliximab	If stopped by 20 weeks, full term infant can have a normal vaccination schedule. If used till term, avoid live vaccinations in infant vaccination schedule until 6 months of age
Ixekizumab	If used to treat severe maternal disease in the third trimester, avoid all live vaccines in the infant vaccination schedule until 6 months of age.
Risankizumab	Not included in BSR guidance
Secukinumab	If used to treat severe maternal disease in the third trimester, avoid all live vaccines in the infant vaccination schedule until 6 months of age.
Ustekinumab	If used to treat severe maternal disease in the third trimester, avoid all live vaccines in the infant vaccination schedule until 6 months of age.
JAK inhibitors	Not applicable. Contraindicated in pregnancy.

Peri-operative supportive information

Drug	Dosing interval	Period in which surgery should be scheduled (relative to last drug dose administered)	One mean half-life	Five half-lives
Adalimumab	Every 2 weeks	Week 3	14 days	70 days
Apremilast	Twice daily	Can continue if not high risk	9 hours	~2 days
Bimekizumab	Every 4 weeks	Week 5	30 days	150 days
Certolizumab pegol	Every 2 weeks Every 4 weeks	Week 3 Week 5	14 days	70 days
Etanercept	Weekly or twice weekly	Week 2	3 days	15 days
Golimumab	Every 4 weeks	Week 5	14 days	70 days
Guselkumab	Every 8 weeks	Week 9	17 days	85 days
Infliximab IV	Every 4, 6 or 8 weeks	Week 5, 7 or 9	9 days	45 days
Ixekizumab	Every 4 weeks	Week 5	14 days	70 days
Risankizumab	Every 12 weeks	Week 13*	29 days	145 days
Secukinumab	Every 4 weeks	Week 5	30 days	150 days
Tofacitinib	Twice daily	Day 4**	3 hours	15 hours
Upadacitinib	Once daily	Day 4**	14 hours	3 days
Ustekinumab	Every 12 weeks	Week 13	21 days	105 days

*No published guidance available, recommendation based on half-life and dosing interval

**Tofacitinib/Upadicitinib is rapidly eliminated but treatment effects do not reverse fully within 2 weeks after discontinuation, indicating a longer duration of pharmacodynamic activity compared to the half-life (8). Although not stated in summary of product characteristics this may be applicable to all JAK inhibitors due to mechanism of action. Prescribers may wish to consider longer time to surgery, i.e. Week 2.

Appendices

1. Governance information for Guidance document

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CHANGE RECORD

Date	Lead Author	Change	Version No.
January 2025	Sanjiv Nandwani	Initial Version	1
			2
			3

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			5

2.You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.

e.g. supporting documents for implementation of guideline, patient information, specific monitoring requirements for secondary and primary care clinicians, dosing regimen/considerations according to weight and/or creatinine clearance