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Norfolk and Waveney Integrated Care System

Psoriatic arthritis high-cost drug pathway 2023

Norfolk and Waveney Integrated Care System

1. Table of Contents

2. Document Control Sheet

Name of document:	Psoriatic arthritis high-cost drug pathway 2023
Description of policy	NWICB high-cost drug pathway for Psoriatic Arthritis
Version	1.0
Scope	
Prepared by	Medicine optimisation team With input/advice from specialists at NNUH, QEH & JPH
Impact Assessment (Equalities and Environmental)	
Other relevant approved documents	
Evidence base / Legislation	Level of Evidence: ~~A. based on national research-based evidence and is considered best evidence~~ **B. mix of national and local consensus** ~~C. based on local good practice and consensus in the absence of national research based information.~~
Dissemination	Is there any reason why any part of this document should not be available on the public web site? ~~Yes~~ / **No**
Approved by	N&WICB Therapeutics advisory group
Authorised by	N&WICB Therapeutics advisory group
Review date and by whom	July 2025
Date of issue	07/07/2023

2.1 Revision History

Revision Date	Summary of changes	Author(s)	Version Number
08/11/2022	Initial draft of local policy and inclusion of new NICE TAs	A. Charlwood, M. Sully	0.1
08/02/2022	Amended to reflect advice from specialists, inclusion of summary document	As above & local specialists	0.2
18/05/2023	Minor amendments to summary document & pregnancy info. Inclusion of JAK inhibitor MHRA warning	As above	0.3
30/06/2023	Added Adalimumab biosimilar weekly dose escalation as agreed locally. Agreed by TAG.	As above	1

2.2 Approvals

This document requires the following approvals either individual(s), group(s) or board.

Name	Title	Date of Issue	Version Number
Norfolk & Waveney ICB Therapeutics Advisory Group		07/06/2023	1.0

3. Introduction

3.1 Relevant NICE technology Appraisals

Technology Appraisal*	Title
TA199	Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis
TA220	Golimumab for the treatment of psoriatic arthritis
TA340	Ustekinumab for treating active psoriatic arthritis
TA433	Apremilast for treating active psoriatic arthritis
TA445	Certolizumab pegol and Secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs
TA537	Ixekizumab for treating active psoriatic arthritis after inadequate response to DMARDs
TA543	Tofacitinib for treating active psoriatic arthritis after inadequate response to DMARDs
TA768	Upadacitinib for treating active psoriatic arthritis after inadequate response to DMARDs
TA803	Risankizumab for treating active psoriatic arthritis after inadequate response to DMARDs
TA815	Guselkumab for treating active psoriatic arthritis after inadequate response to DMARDs

*NICE recommendations **also apply to biosimilar products of the technologies** that have a marketing authorisation, allowing the use of the biosimilar for the same indication.

3.2 Pathway scope

This pathway is to be used to guide the initiation and maintenance of high-cost drugs in the management of Psoriatic arthritis and have been written using up to date published NICE Technology Appraisals (TAs) and evidence-based medicine.

The pathway includes:

- TNF inhibitors (TNFi): Adalimumab, etanercept, infliximab, golimumab & certolizumab
- Interleukin-12 & 23 inhibitors (IL-12/23i): Ustekinumab
- Interleukin-17A inhibitor (IL-17Ai): Ixekizumab & Secukinumab
- Interleukin-23 inhibitor (IL-23i): Guselkumab & Risankizumab
- JAK inhibitors (JAKi): Tofacitinib & upadacitinib
- PDE4 inhibitor (PDEF4i): Apremilast

Drugs should be used in accordance with the relevant TA. The links are included in this document. Inclusion will be allowed for any new high-cost drugs that are approved by NICE prior to review of the pathway, provided that the relevant local "New Medicines" Policy and process has been followed. Those drugs should be used in accordance with the relevant NICE TA. The NICE recommendations also apply to biosimilar drugs, where marketing authorisations allow use of the biosimilar for the indication specified in the relevant NICE TA.

3.3 Introduction to Psoriatic arthritis

Psoriatic arthritis is an inflammatory arthritis affecting the joints and connective tissue and is associated with psoriasis of the skin or nails. The prevalence of psoriasis in the general population is estimated at 2–3%. The prevalence of inflammatory arthritis in people with psoriasis is estimated at up to 30%. At least 20% of people with psoriasis have severe psoriatic arthritis with progressive joint lesions. Psoriatic arthritis is a progressive disorder ranging from mild synovitis to severe progressive erosive arthropathy. People with psoriatic arthritis presenting with oligoarticular disease progress to polyarticular disease and a large percentage develop joint lesions and deformities, which progress over time. Despite clinical improvement with current DMARD treatment, joint damage has been shown radiologically in up to 47% of people with psoriatic arthritis at a median interval of 2 years[1].

4. Before initiating high-cost drug treatment

4.1 Exploring further benefit from non-biological therapy

Strategies to optimize the use of systemic non-biological therapies prior to the initiation of biologic therapy, for example:

- Adjusting folic acid prescribing to improve tolerance to oral methotrexate
- Where clinically suitable, consider switching to subcutaneous methotrexate, to address potential gastrointestinal adverse effects, poor compliance, or concerns regarding absorption of oral formulation.
- Where appropriate, maximum intensification of combination therapy using maximum tolerated doses.

4.2 Inclusion criteria

- The person has peripheral arthritis with three or more tender joints and three or more swollen joints,

and

- The psoriatic arthritis has not responded to adequate trials of at least two standard disease-modifying antirheumatic drugs (DMARDs), administered either individually or in combination.

4.3 Pharmacovigilance

To support ongoing pharmacovigilance of biologics, including biosimilars, must be prescribed by brand name. Any new biological drug, including biosimilars, requires pharmacovigilance, and the black triangle denotes further monitoring.

The University of Aberdeen facilitates a registry on behalf of the BSR that collects data for the long-term outcomes of treatment with biologics for PsA. NICE noted the importance of these in collecting data and supported including outcomes specific to psoriatic arthritis in a suitable registry so that specific information about these treatments in psoriatic arthritis can be captured.

5. Initiating high-cost drug treatment

5.1 Choice of initial therapy

Within the Norfolk & Waveney ICS resources should be utilized as carefully as possible, to allow more patients to access these high-cost treatments as demand rises. The least priced treatment should be chosen if more than one is appropriate (taking into account patient factors, administration costs, dosage and price per dose). MHRA recommendations regarding prescribing biosimilars can be found here.

The least priced product, whether it be a biosimilar or an original, should be prescribed once a biologic treatment has been decided upon. Local guidelines, clinical judgement, and the overall value proposition provided by the various medications should be taken into consideration. The justification for the decision should be documented.

To support decision making, please refer to Appendix 1: High-Cost Drugs Algorithm.

5.1.1 Adalimumab

Adalimumab is the preferred first line choice for biologic therapy in PsA, unless contraindicated. It is clinically effective in psoriatic arthritis and psoriasis. It is relatively low cost, has a well-established safety profile and has a reduced dose interval relative to Etanercept.

5.1.2 Ustekinumab

Ustekinumab (TA340) is only recommended for use after unsuccessful TNFi treatment, or when an TNFi would be used but is contraindicated.

5.2 Treatment by domain

The following statements are from the 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs[2].

5.2.1 Psoriatic arthritis with axial disease

For patients with active psoriatic axial disease, any TNFi, JAK inhibitor, or IL-17i are appropriate options[2].

5.2.2 Psoriatic arthritis with extra-articular manifestations (psoriasis, uveitis, inflammatory bowel disease)

Where a person has associated conditions alongside their psoriatic arthritis, such as psoriasis, uveitis and/ or IBD, a multidisciplinary and multispecialty approach should be taken for their care including timely discussions prior to systemic treatment changes. Be aware of other licensed indications and option for differential dosing of common medications in different indications to optimize doses for each individual[2].

5.3 Adalimumab biosimilar weekly dose escalation (local agreement)

As per local agreement (TAG - May 2023), patients on the usual dose of adalimumab 40mg every 2 weeks subcutaneously, who have experienced loss of efficacy with subtherapeutic trough adalimumab levels. Note, the following exclusions apply:

- patients on the originator (Humira)
- patients who have anti-drug antibodies

Published data is limited, however this approach is becoming increasingly used in practice as an intermediate step – the use will be off label in some circumstances (specifically, in combination with methotrexate), and in these cases should be discussed with the patient and be documented in the patient notes.

5.3.1 Ongoing management

The benefits and risks of continued 40 mg weekly therapy should be carefully reconsidered in a patient with an inadequate response after the increase in dosage. If adequate response is achieved with 40 mg every week, the dosage may subsequently be reduced to 40 mg every other week.

6. Switching to a second biologic in psoriatic arthritis

As additional biosimilar drugs become accessible, there have been and are still widespread shifts to these treatments. There is virtually little evidence in favour of or against switching, and these decisions are more closely tied to finances than formal efficacy. This advice is based on the information in the 2018 BSR factsheet on biosimilars. The guideline recommends that people can switch back to the originator if they lose efficacy or there are safety issues with the new biosimilar.

PsA sufferers frequently experience a lack of response to or a loss of response to advanced therapy. Consequently, no suggestions for a particular treatment class are offered. Generally, after primary failure, switching drug class would be preferred over one with the same mechanism of action. For secondary failure, the same manner of intervention may be the best course of action following secondary failure.

7. Contraindications, special warnings, and precautions for treatment with drugs

See **appendix 2** for full breakdown.

7.1 MHRA warnings

7.1.1 Apremilast

Be aware of the MHRA warning circulated in January 2017 stating:

"There is an increased risk that some patients may experience psychiatric symptoms with apremilast, including depression and suicidal thoughts. Stop treatment if patients have new psychiatric symptoms or if existing symptoms worsen."

The MHRA advice for Apremilast is as follows:

- "Apremilast is associated with an increased risk of psychiatric symptoms, including depression, suicidal thoughts, and suicidal behaviours

- 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
- stop treatment if patients experience new psychiatric symptoms or if existing symptoms get worse
- advise patients to inform a healthcare professional if they notice changes in their mood"

7.1.2 Janus kinase (JAK) inhibitors

There have been several MHRA warnings since 2020 for individual JAK inhibitors. In March 2023 the MHRA released information for risk minimisation which has been previously recommended for tofacitinib & upadacitinib, would now apply to all JAK inhibitors. Points of interest[3] include:

- following a review, these risks are considered class effects across JAK inhibitors used for chronic inflammatory disorders and therefore it is advised to avoid prescribing these medicines unless there are no suitable alternatives in patients with the following risk factors:
    - age 65 years or older
    - current or past long-time smoking
    - other risk factors for cardiovascular disease or malignancy
- use caution if prescribing in patients with risk factors for VTE other than those listed above (see below for more details)

It is recommended to read the full guidance here for the full details on caution

8. Blueteq

Blueteq forms which comply with this pathway are available. Funding approval for the tariff excluded high-cost drugs will **be required by submission of the relevant Blueteq form prior to treatment administration for all drugs except Adalimumab biosimilar.** The Blueteq forms contain a list of relevant criteria that the patient must meet to secure funding. Any patients who do not meet these criteria will require an individual funding request, further information found on Knowledge Anglia.

9. Route of administration, dose & initial review interval

Therapy should be provided by subcutaneous (SC) injection, rather than intravenous (IV) infusion where possible, to enable transfer of services to home care providers. Treatment reviews post initiation should take place within the recommended period to establish effectiveness. Therapy should only be continued if there is the improvement as defined by NICE TA. Refer to SPC (linked in Appendix 2) for specific loading dose frequency.

Drug	Route of administration	Review of response after initiation	Frequency post loading
Adalimumab biosimilar	SC injection	12 weeks	Every 2 weeks
Apremilast	Oral	16 weeks	30mg twice daily
Certolizumab	SC injection	12 weeks	200mg every 2 weeks
Etanercept biosimilar	SC injection	12 weeks	Twice per week
Golimumab	SC injection	12 weeks	Every 4 weeks
Guselkumab	SC injection	16 weeks	Every 8 weeks
Infliximab biosimilar	IV infusion	10 weeks	Every 8 weeks
Ixekizumab	SC injection	16 weeks	Every 4 weeks
Risankizumab	SC injection	16 weeks	150mg every 3 months
Secukinumab	SC injection	16 weeks	Every 4 weeks
Tofacitinib	Oral	12 weeks	5mg twice daily
Upadacitinib	Oral	12 weeks	15mg once daily
Ustekinumab	SC injection	12 weeks	Every 12 weeks

10. Dose escalation

There are no national guidelines recommending the use of dose escalation in psoriatic arthritis.

Where individual exceptionality to the routine commissioning policy can be demonstrated, an individual funding request application must be made to request funding for dose escalation. Routine commissioning of dose escalation will require a business case to be submitted to commissioners.

11. Switching biologics

The four main kinds of biologic therapeutics target various cytokines or have varied affinities or avidities for the same cytokine. One of these cytokines is likely the main initiator of any patient's disease. Therefore, a patient's responsiveness to other biological agents in a different class cannot be predicted based on their lack of response to one biological agent used to treat psoriasis.

Even though all biologic medications are quite effective in the short term, biologic drugs have an annual attrition rate of ~20% or more[4], necessitating modifications in therapy for longer term disease control for a condition that is a lifelong condition. When practicable, boosting the dose of biologic therapy in adults may be considered when an unsatisfactory first response may be due to insufficient drug dosing, such as in obese patients or when psoriasis relapses throughout the treatment cycle. Be aware that there may be a higher risk of infection as a result.

BAD biologic therapy for psoriasis guidelines provide extremely good resources to support clinicians with switching between biologics. Considerations for safety should be weighed against the possibility of a disease flare-up. If a change in biologic agent is needed, NICE psoriasis guidance advises to consider changing to an alternative biological drug in adults if:

- The psoriasis does not respond adequately to a first biological drug as defined in NICE technology appraisals (**primary failure**) **or**
- The psoriasis initially responds adequately but subsequently loses this response, (**secondary failure**) **or**
- The first biological drug cannot be tolerated or becomes **contraindicated**.

For adults in whom there is an inadequate response to a second biological drug, seek supra-specialist advice from a clinician with expertise in biological therapies. Local policy allows for supra-specialist providers to prescribe a fourth biologic where secondary failure occurs.

12. Perioperative infection risk management

By temporarily discontinuing a patient's biologic medication, the chance of a post-operative infection should be reduced, but this should be carefully weighed against the risk of a peri-operative flare. Consider halting medication 3-5 half-lives before surgery if there is a high chance of infection or could cause substantial harm. As shown in the table below, some biologics need up to 33 weeks to achieve 3-5 half lives. Locally, there are joint guidelines for the management of interruption of biologic therapies for elective surgery in adults and children, produced by the rheumatology departments across the NWICB, which suggest a shorter interruption of biologic treatment may be appropriate[5]. For further information refer to the guidance linked.

Drug	Mean half-life as per SPC	Time to stop treatment prior to surgery (3-5 half-lives)	Local guidelines; Time between last dose and surgery
Tofacitinib	3 hours	1 day	Stop 2 days prior to surgery
Upadacitinib	12 hours	1.5-3 days	No guidance
Etanercept	3 days	9- 15 days	2 weeks
Infliximab	8-9.5 days	4-7 weeks	5, 7 or 9 weeks
Golimumab	12 days	5-9 weeks	5 weeks
Adalimumab	2 weeks	6-10 weeks	3 weeks
Certolizumab pegol	14 days	6-10 weeks	3 weeks
Ixekizumab	13 days	6-10 weeks	10 weeks
Guselkumab	15-18 days	7-13 weeks	5-9 weeks
Risankizumab	28.5 days	12-20 weeks	5 weeks
Ustekinumab	15-32 days	7-23 weeks	13 weeks
Secukinumab	18-46 days	8-33 weeks	12 weeks

Post-operatively, once infection has been ruled out and the wound has healed, treatment should resume. Consider maintaining treatment in situations when there is a low chance of infection or a high risk of illness flare-up. If possible, surgery might be planned for a period when it is anticipated that drug levels will be low.

13. Vaccinations

Prior to initiating biologic treatment, vaccination requirements should be evaluated and updated in accordance with Department of Health guidance.

Do not administer live vaccinations to individuals receiving biologic treatment. Stop biologic medication for at least 12 months prior to administering live vaccinations, including the herpes zoster (shingles) vaccine. Expert opinion suggested, however, that 12 months may not be necessary for all biologics, and where live vaccinations must be considered, expert advice should be sought and/or the individual specifications in the SPC, where timelines are stated explicitly for some of the biologic drugs, should be reviewed. Generally, biologic treatment may be started four weeks after a live vaccination is administered. Consult the drug's SPC and the Green Book for more information.

The Green Book and the clinical risk category 'immunosuppression' should be used to determine immunisation needs during treatment. It is safe to provide inactivated vaccinations simultaneously with biologic treatment. To promote effective immune responses, inactivated vaccines should preferably be delivered at least 2 weeks prior to commencing treatment.

Prior to biologic treatment, patients should obtain yearly influenza vaccination (intramuscular only), pandemic influenza vaccination when suggested, and pneumococcal immunisation. Clinicians should be aware that TNF antagonist monotherapy may result in diminished antibody responses to influenza vaccination, and that TNF antagonists in combination with methotrexate (alone) may result in diminished antibody responses to pneumococcal vaccine.

13.1 New-borns to mothers who have received biological therapy

New-borns (up to 6 months of age) whose mothers received biologic therapy after 16 weeks' gestation. Patients should be counselled about the need of avoiding live immunizations and the potential implications for international travel.

14. Pregnancy

There is limited data for safety of biologic medicines in pregnancy and breastfeeding. The decision to continue biologic medicines throughout pregnancy must be individualised. This should consider the various therapies, severity of the mother's health prior to therapy, risk of a disease flare if therapy is discontinued, and the impact of a disease flare on the mother and unborn child. This should be discussed by a multi-disciplinary team. Patients who discontinue treatment during pregnancy should resume biological therapy as soon as possible following delivery.

14.1 Choice of therapy for patients planning to conceive

Adalimumab is locally recommended as the first line option for patients who are planning to conceive in the future. Adalimumab biosimilar provides the best value whilst being safe during the first two trimesters. It is vital the patient is aware that they must flag any pregnancy with the responsible clinician, so safety during the third trimester can be managed (either through temporary discontinuation or a switch to Certolizumab).

See the table below for further details on specific biologics in the different stages of pregnancy, information collated from the BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding[6], and SPC of the relevant biologic.

	Compatible with trimester		
Drug	1st	2nd	3rd
Certolizumab pegol	Yes	Yes	Yes
Adalimumab	Yes	Yes	No
Etanercept	Yes	Yes	No
Infliximab	Yes	Stop at 16 weeks	No
Upadacitinib	No		
Tofacitinib	No		
Ixekizumab	Limited data		
Apremilast	No, use effective contraceptive during treatment.		
Ustekinumab	Data unavailable		
Secukinumab	Data unavailable		
Risankizumab	Data unavailable		
Guselkumab	Data unavailable		

14.2 Breastfeeding

There is little information available regarding the excretion of biologics in breast milk. Immunoglobulins are excreted in human breast milk, so a risk to a child cannot always be ruled out. The decision to breastfeed or continue/discontinue therapy should consider both the benefits of breastfeeding to the infant and the benefits of therapy to the mother.

See the table below for further details on specific biologics in breastfeeding, information is taken from the SPC of the relevant biologic. Where no data or recommendation is provided, it would be appropriate to use the "Time to stop treatment prior to surgery" listed in section 11 to determine time between discontinuing treatment and starting breastfeeding.

Biologic	Compatible with Breastfeeding
Adalimumab	Yes
Certolizumab pegol	Yes
Etanercept	Limited data - Balance risk vs benefits
Infliximab	Wait 6 months until after stopping to breastfeed
Golimumab	Wait 6 months until after stopping to breastfeed
Secukinumab	Wait 20 weeks until after stopping to breastfeed
Ustekinumab	Wait 15 weeks until after stopping to breastfeed
Ixekizumab	No data
Risankizumab	No data
Guselkumab	No data
Tofacitinib	No - Contraindicated
Upadacitinib	No - Contraindicated
Apremilast	No - Contraindicated

15. Correspondence

15.1 Information to be included in correspondence from secondary to primary care:

- Main diagnosis/diagnoses
- Date(s) of intervention

- Secondary diagnosis/diagnoses
- Date of last examination, with findings & timing of next planned review/ contact with secondary care
- Current medical therapy including any previous treatments within pathway (including non-biologics)
- Recommended length of current medical therapy

15.2 Information to be included in correspondence from primary to secondary care:

- Date last prescription issued
- All current and recent medications.
- Functional impact e.g., impact on employment, family, and social functioning
- Any newly diagnosed co-morbidities

16. References

1. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis | Guidance | NICE. Accessed August 8, 2022. https://www.nice.org.uk/guidance/ta199/chapter/2-Clinical-need-and-practice

2. Tucker L, Allen A, Chandler D, et al. The 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs. *Rheumatology*. Published online May 31, 2022:keac295. doi:10.1093/rheumatology/keac295

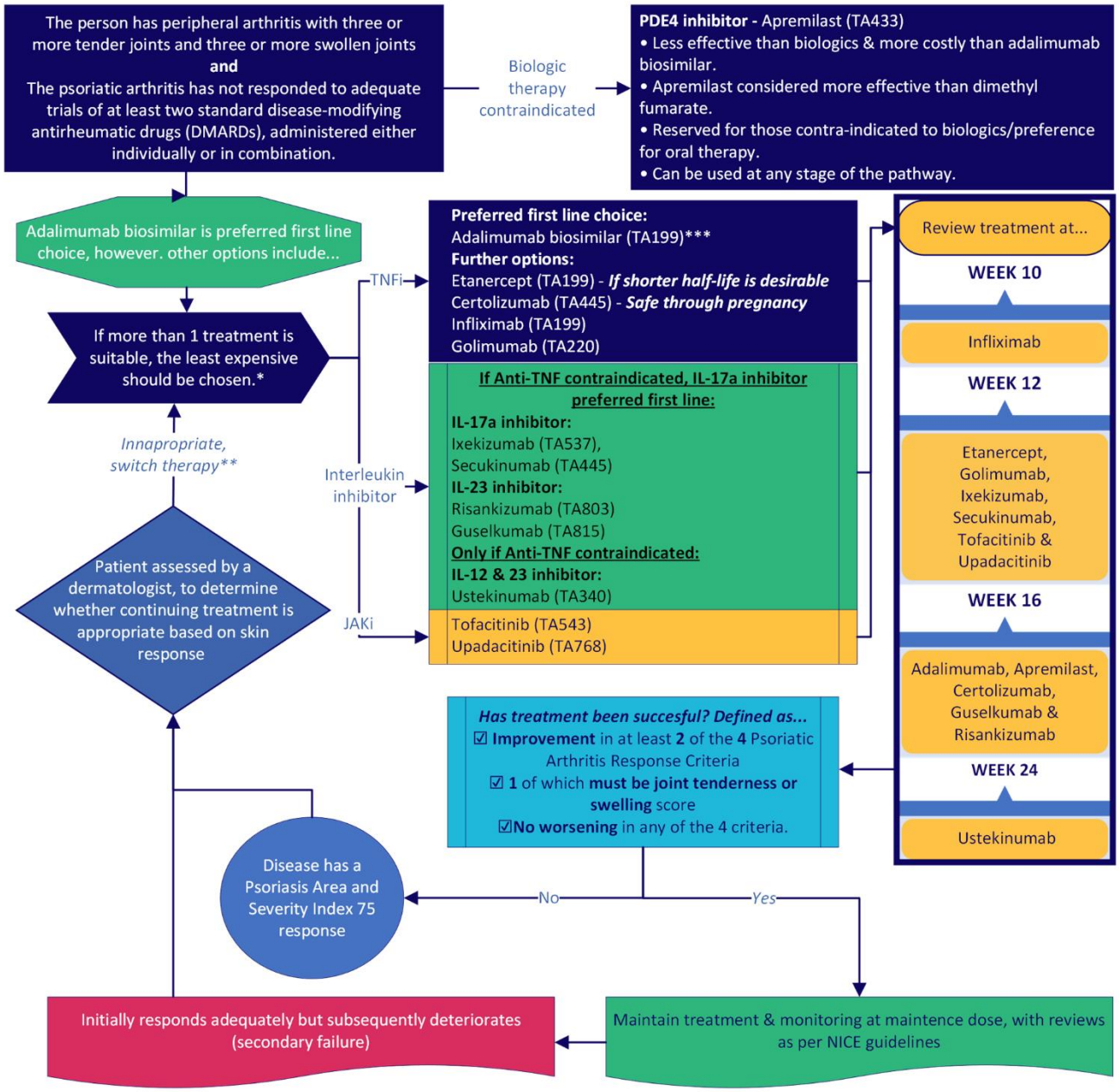
3. Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality - GOV.UK. Accessed May 18, 2023. https://www.gov.uk/drug-safety-update/janus-kinase-jak-inhibitors-new-measures-to-reduce-risks-of-major-cardiovascular-events-malignancy-venous-thromboembolism-serious-infections-and-increased-mortality

4. Warren RB, Smith CH, Yiu ZZN, et al. Differential Drug Survival of Biologic Therapies for the Treatment of Psoriasis: A Prospective Observational Cohort Study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). *Journal of Investigative Dermatology*. 2015;135(11):2632-2640. doi:10.1038/jid.2015.208

5. Nicola Kerrigan. Interruption-of-Biologic-Therapy-JCG0030-V5.pdf. Published online August 25, 2022. https://www.nnuh.nhs.uk/publication/interruption-of-biologic-therapy-jcg0030-v5/

6. Flint J, Panchal S, Hurrell A, et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. *Rheumatology*. 2016;55(9):1693-1697. doi:10.1093/rheumatology/kev404

17. Appendix 1 – High-Cost Drugs Pathway



* Choice of therapeutic agent as first line

•Although Adalimumab biosimilar is the least costly option, there are numerous situations when this option would be inappropriate. No drug class is recommended in preference to another (As per BSR guidelines). As per NICE guidance, treatment should normally be started with the least expensive drug (considering the dose required, price per dose and any additional administration costs).

** Switching to a second biologic in psoriatic arthritis

•PsA sufferers frequently experience a lack of response to or a loss of response to advanced therapy. Consequently, no suggestions for a particular treatment class are offered. **Generally, after primary failure, switching drug class would be preferred over one with the same mechanism of action**. For secondary failure, the same manner of intervention may be the best course of action following secondary failure. *See table on reverse of summary document for further information on available options.*

*** Weekly Adalimumab escalation

•As per local agreement (TAG - May 2023), patients on the usual dose of adalimumab 40mg every 2 weeks subcutaneously, who have experienced loss of efficacy with subtherapeutic trough adalimumab levels. Note, the following exclusions apply; patients on the originator (Humira) & patients who have anti-drug antibodies. See full pathway for further details

Published MHRA Warnings for Specific Agents:

- **Apremilast** (Otezla®): risk of suicidal thoughts and behaviour (January 2017)
- **All JAK inhibitors:** increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality (April 2023)

18. Appendix 2 – Contraindications, special warnings, and precautions for treatment with drugs

	Contraindications	Special warnings and precautions	Undesirable Effects
TNFis SPCs: Adalimumab, Certolizumab, Etanercept, Infliximab & Golimumab	• Hypersensitivity to active substance, to other murine proteins, or to any product excipients. • Patients with/at risk of severe infections such as tuberculosis sepsis, abscesses, and opportunistic infections. • Patients with moderate or severe heart failure (NYHA class III/IV) (see sections 4.4 and 4.8).	• Patients taking TNF-antagonists are more susceptible to serious infections • History of Hepatitis B • Comorbidity of demyelinating disorders, review people who have a first-degree relative with demyelinating disease. • NYHA class I and II cardiac failure.	• May increase the risk of infections & reactivate latent infections • May increase the risk of malignancy • Demyelination • Heart failure • Hepatobiliary events • Haematologic reactions
Interleukin-23 inhibitor SPCs: Risankizumab & Ustekinumab	• Hypersensitivity to the active substance or to any of the excipients • Clinically important, active infection (e.g., active tuberculosis)	• No specific concerns relating to comorbidities	• May increase the risk of infections & reactivate latent infections • May increase the risk of malignancy • In some cases, several days after treatment, anaphylaxis and angioedema have occurred
Interleukin-17A inhibitor SPCs Ixekizumab & Secukinumab	• Hypersensitivity to the active substance or to any of the excipients • Active Crohn's disease • Clinically important active infections (e.g. active tuberculosis)	• Consult with gastroenterology specialist before using in patients with inflammatory bowel disease	• May increase the risk of infections & reactivate latent infections • May increase the risk of malignancy • In some cases, several days after treatment, anaphylaxis and angioedema have occurred
JAK inhibitors SPC Tofacitinib & Upadacitinib	• Hypersensitivity to the active substance or to any of the excipients • Active tuberculosis (TB), serious infections such as sepsis, or opportunistic infections • Severe hepatic impairment • Pregnancy and lactation	• Use in patients over 65 years of age • History of venous thromboembolism • Risk of serious infection • Viral reactivation • Cardiovascular risk factors (including past smokers)	• Hypertension • Increased infection frequency • Gastrointestinal side effects • Rash • Oedema peripheral
PDE4 inhibitor SPC Apremilast	• Hypersensitivity to the active substance(s) or to any of the excipients • Pregnancy	• Reduce dose in severe renal impairment • Increased risk of psychiatric disorders (e.g., insomnia, depression)	• Diarrhoea, nausea, and vomiting • Unexplained weight loss

19. Appendix 3 - Psoriatic Arthritis high cost drugs summary document [2,7–9]

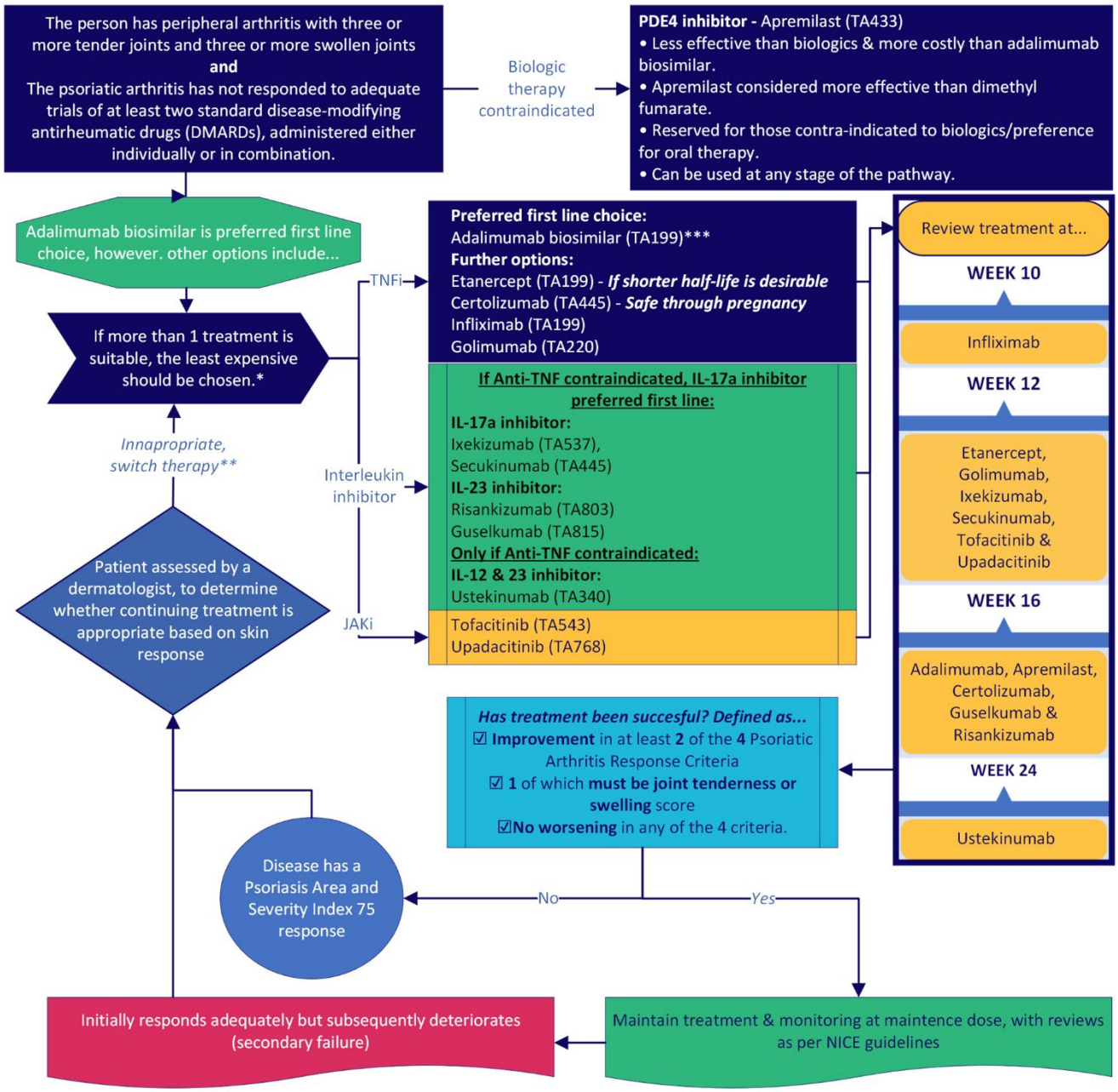
Psoriatic Arthritis high cost drugs summary

Drug	Relative cost	American College of Rheumatology 50% response		Psoriasis area and severity index 75% response		Minimal disease activity rates at week 24	Licence in PsA	P3 data in AS/AxSpA	Licence in AS/AxSpA	P3 data in IBD	Licence in IBD	Licence in uveitis	Enthesitis efficacy	Dactylitis efficacy	Contra-indications	Key safety issues
		Week 12-16	Week 24	Week 12–16	Week 24											
Adalimumab (ADA)		3% 33%	6% 40%	4% 49%	1% 59%	6% 36%	✓	✓	✓	✓	✓	✓	N/A	N/A	NY class 3/4 heart failure	Demyelination, non-melanoma skin cancer, infections
Infliximab (INF)		2% 39%	4% 41%	2% 65%	1% 60%		✓	✓	✓	✓	✓	X	✓	✓		
Etanercept (ETN)		4% 40%	4% 37%		3% 23%		✓	✓	✓	X	X	X	N/A	N/A	NY class 3/4 heart failure	Demyelination, non-melanoma skin cancer, infections
Upadacitinib (UPAD)		13% 38%	19% 52%	21% 63%		12% 37%	✓	✓	X	✓ (UC)	✓ (UC)	X	✓	X	Severe hepatic impairment	
Tofacitinib (TOFA)		10% 28%		15% 43%		19% 26%	✓	✓	X	✓ (UC)	✓ (UC)	X	✓ (pooled)	✓ (pooled)	Severe hepatic impairment	Herpes zoster, VTE, malignancy risk, MACE
Apremilast (APR)		7% 13%	4% 20%	6% 22%	5% 21%		✓	X	X	X	X	X	✓ (pooled)	✓ (pooled)		Suicidal thought and behaviour
Ixekizumab (IXE)		5% 34%	15% 40%	8% 75%	10% 71%	15% 30%	✓	✓	✓	X	X	X	✓ (pooled)	✓		IBD, fungal & bacterial infections
Secukinumab (SEC)		9% 40%	9% 46%	13% 65%	32% 72%	15% 41%	✓	✓	✓	X	X	X	✓	✓		IBD, fungal & bacterial infections
Certolizumab pegol (CZP)		12% 35%	15% 42%	17% 43%	20% 56%	6% 33%	✓	✓	✓	✓ (CD)	✓ (CD)	X	✓	✓	NY class 3/4 heart failure	Demyelination, non-melanoma skin cancer, infections
Ustekinumab (UST)			9% 26%	9% 50%	11% 60%		✓	✓	✓	✓	✓	X	✓	✓		Exfoliative dermatitis
Risankizumab (RSK)		7% 18%	9% 26%				✓	X	X	✓ (CD)	X	X	✓	✓		Infections
Golimumab (GOL)		2% 29%	4% 35%	3% 49%	1% 59%	0% 0%	✓	✓	✓	✓ (UC)	✓ (UC)	X	✓	✓	NY class 3/4 heart failure	Demyelination, non-melanoma skin cancer, infections
Guselkumab (GUS)			14% 31%		23% 79%	11% 23%	✓	X	X	✓ (CD)	X	X	✓ (pooled)	✓ (pooled)		

Information regarding licencing & published evidence

- The information above (adapted from the 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs[1]) aims to provide a brief overview of licenced indications & evidence from phase 3 trials for indications other than psoriatic arthritis. Local pathways should be consulted for specific co-morbidities to confirm that any option is appropriate & commissioned.

1. Tucker L, Allen A, Chandler D, et al. The 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs. *Rheumatology*. 2022;61(9):e255-e266. doi:10.1093/rheumatology/keac295



* Choice of therapeutic agent as first line

- Although Adalimumab biosimilar is the least costly option, there are numerous situations when this option would be inappropriate. No drug class is recommended in preference to another (As per BSR guidelines). As per NICE guidance, treatment should normally be started with the least expensive drug (considering the dose required, price per dose and any additional administration costs).

** Switching to a second biologic in psoriatic arthritis

- PsA sufferers frequently experience a lack of response to or a loss of response to advanced therapy. Consequently, no suggestions for a particular treatment class are offered. **Generally, after primary failure, switching drug class would be preferred over one with the same mechanism of action**. For secondary failure, the same manner of intervention may be the best course of action following secondary failure. *See table on reverse of summary document for further information on available options.*

*** Weekly Adalimumab escalation

- As per local agreement (TAG - May 2023), patients on the usual dose of adalimumab 40mg every 2 weeks subcutaneously, who have experienced loss of efficacy with subtherapeutic trough adalimumab levels. Note, the following exclusions apply; patients on the originator (Humira) & patients who have anti-drug antibodies. See full pathway for further details

Published MHRA Warnings for Specific Agents:

- **Apremilast** (Otezla®): risk of suicidal thoughts and behaviour (January 2017)
- **All JAK inhibitors:** increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality (April 2023)

20. Appendix 4 – NICE technology appraisal detail

Technology Appraisal	Title
TA199	Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis 1. Etanercept, infliximab and adalimumab are recommended for the treatment of adults with active and progressive psoriatic arthritis when the following criteria are met. 1.1. The person has peripheral arthritis with three or more tender joints and three or more swollen joints, **and** 1.2. The psoriatic arthritis has not responded to adequate trials of at least two standard disease-modifying antirheumatic drugs (DMARDs), administered either individually or in combination. 2. Treatment as described in 1 should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individual patients because of differences in the method of administration and treatment schedules. 3. Etanercept, adalimumab or infliximab treatment should be discontinued in people whose psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks. An adequate response is defined as an improvement in at least two of the four PsARC criteria, (one of which has to be joint tenderness or swelling score) with no worsening in any of the four criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks but whose PsARC response does not justify continuation of treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis). 4. When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect person's responses to components of the PsARC and make any adjustments they consider appropriate.
TA220	Golimumab for the treatment of psoriatic arthritis 1. Golimumab is recommended as an option for the treatment of active and progressive psoriatic arthritis in adults only if: 1.1. it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (NICE technology appraisal guidance 199), **and** 1.2. the manufacturer provides the 100 mg dose of golimumab at the same cost as the 50 mg dose. 2. When using the Psoriatic Arthritis Response Criteria (PsARC; as set out in NICE technology appraisal guidance 199), healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.
TA340	Ustekinumab for treating active psoriatic arthritis 1. Ustekinumab is recommended as an option, alone or in combination with methotrexate, for treating active psoriatic arthritis in adults only when: 1.1. treatment with tumour necrosis factor (TNF) alpha inhibitors is contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis and golimumab for the treatment of psoriatic arthritis) or 1.2. the person has had treatment with 1 or more TNF–alpha inhibitors. 2. Ustekinumab treatment should be stopped if the person's psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 24 weeks. An

	adequate response is defined as an improvement in at least 2 of the 4 criteria (1 of which must be joint tenderness or swelling score), with no worsening in any of the 4 criteria. As recommended in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, people whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC response does not justify continuing treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see NICE technology appraisal guidance on ustekinumab for the treatment of adults with moderate to severe psoriasis). 3. When using the Psoriatic Arthritis Response Criteria (PsARC) healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. **4.** People whose treatment with ustekinumab is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue ustekinumab until they and their NHS clinician consider it appropriate to stop.
TA433	Apremilast for treating active psoriatic arthritis 1. Apremilast, alone or in combination with disease-modifying antirheumatic drugs (DMARDs), is recommended as an option for treating active psoriatic arthritis in adults only if: 1.1. they have peripheral arthritis with 3 or more tender joints and 3 or more swollen joints **and** 1.2. their disease has not responded to adequate trials of at least 2 standard DMARDs, given either alone or in combination **and** 1.3. the company provides apremilast with the discount agreed in the patient access scheme. 2. Stop apremilast at 16 weeks if the psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis response Criteria (PsARC), defined as an improvement in at least 2 of the 4 PsARC criteria (including joint tenderness or swelling score) with no worsening in any criteria. If the disease has a Psoriasis Area and Severity Index (PASI) 75 response, a dermatologist should decide whether to continue treatment with apremilast after 16 weeks based on skin response. 3. When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. 4. This guidance is not intended to affect the position of patients whose treatment with apremilast was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.
TA445	Certolizumab pegol and Secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs 1. Certolizumab pegol alone, or in combination with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults only if: 1.1. it is used as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1 and 2) **or** 1.2. the person has had a tumour necrosis factor (TNF)-alpha inhibitor but their disease has stopped responding after the first 12 weeks. 1.3. Certolizumab pegol is only recommended if the company provides it as agreed in the patient access scheme. 2. Secukinumab alone, or in combination with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults only if: 2.1. it is used as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1 and 2) or 2.2. the person has had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks or

	2.3. TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis). 2.4. Secukinumab is only recommended if the company provides it as agreed in the patient access scheme. 3. Assess the response to certolizumab pegol and secukinumab after 12 weeks and 16 weeks of treatment respectively. Only continue treatment if there is clear evidence of response, defined as an improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC), 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC response does not justify continuing treatment should be assessed by a dermatologist, to determine whether continuing treatment is appropriate based on skin response (as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, recommendation 3). 4. When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. 5. This guidance is not intended to affect the position of patients whose treatment with certolizumab pegol and secukinumab was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.
TA537	Ixekizumab for treating active psoriatic arthritis after inadequate response to DMARDs 1. Ixekizumab alone, or with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults, only if: 1.1. it is used as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1 and 2) **or** 1.2. the person has had a tumour necrosis factor (TNF)-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after the first 12 weeks **or** 1.3. TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis). 1.4. Ixekizumab is only recommended if the company provides it according to the commercial arrangement. 2. Assess the response to ixekizumab after 16 weeks of treatment. Only continue treatment if there is clear evidence of response, defined as an improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC), 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC response does not justify continuing treatment should be assessed by a dermatologist, to determine whether continuing treatment is appropriate based on skin response (as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, recommendation 3). 3. When using the PsARC, healthcare professionals should take into account any physical, sensory or learning disabilities or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. 4. When using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score, and make the clinical adjustments they consider appropriate. 5. These recommendations are not intended to affect treatment with ixekizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

TA543	Tofacitinib for treating active psoriatic arthritis after inadequate response to DMARDs 1. Tofacitinib, with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults, only if: 1.1. it is used as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1 and 2) **or** 1.2. the person has had a tumour necrosis factor (TNF)-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks **or** 1.3. TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis). 1.4. Tofacitinib is only recommended if the company provides it according to the commercial arrangement. 2. Assess the response to tofacitinib after 12 weeks of treatment. Only continue treatment if there is clear evidence of response, defined as an improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC), 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC response does not justify continuing treatment should be assessed by a dermatologist, to determine whether continuing treatment is appropriate based on skin response (as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, recommendation 3). 3. When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. 4. When using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score, and make the clinical adjustments they consider appropriate. 5. These recommendations are not intended to affect treatment with tofacitinib that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.
	1.
TA768	Upadacitinib for treating active psoriatic arthritis after inadequate response to DMARDs 1. Upadacitinib, alone or with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults whose disease has not responded well enough to disease-modifying antirheumatic drugs (DMARDs) or who cannot tolerate them. It is recommended only if they have peripheral arthritis with 3 or more tender joints and 3 or more swollen joints and: 1.1. they have had 2 conventional DMARDs and at least 1 biological DMARD **or** 1.2. TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis). 1.3. Upadacitinib is recommended only if the company provides it according to the commercial arrangement. 2. Assess the response to upadacitinib after 12 weeks of treatment. Only continue treatment if there is clear evidence of response. This is defined as an improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC), 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria. If PsARC response does not justify continuing treatment but there is a Psoriasis Area and Severity Index (PASI) 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response. 3. Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the PsARC and make any appropriate adjustments. 4. Take into account how skin colour could affect the PASI score and make any appropriate adjustments.

	5. These recommendations are not intended to affect treatment with upadacitinib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.
TA803	Risankizumab for treating active psoriatic arthritis after inadequate response to DMARDs 1. Risankizumab, alone or with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults whose disease has not responded well enough to disease-modifying antirheumatic drugs (DMARDs) or who cannot tolerate them. It is recommended only if they have: 1.1. peripheral arthritis with 3 or more tender joints and 3 or more swollen joints **and** 1.2. moderate to severe psoriasis (a body surface area of at least 3% affected by plaque psoriasis and a Psoriasis Area and Severity Index [PASI] score greater than 10) **and** 1.3. had 2 conventional DMARDs and at least 1 biological DMARD. 1.4. Risankizumab is recommended only if the company provides it according to the commercial arrangement. 2. Assess the response to risankizumab from 16 weeks. Stop risankizumab if psoriatic arthritis has not responded adequately using the Psoriatic Arthritis Response Criteria (PsARC; an adequate response is an improvement in at least 2 of the 4 criteria, 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria). If PsARC response does not support continuing treatment but there is a PASI 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response. 3. If risankizumab is one of a range of suitable treatments, including guselkumab, choose the least expensive (taking into account administration costs, dosage, price per dose and commercial arrangements). 4. Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the PsARC, and make any adjustments needed. 5. Take into account how skin colour could affect the PASI score and make any adjustments needed. 6. These recommendations are not intended to affect treatment with risankizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.
TA815	Guselkumab for treating active psoriatic arthritis after inadequate response to DMARDs 1. Guselkumab, alone or with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults whose disease has not responded well enough to disease-modifying antirheumatic drugs (DMARDs) or who cannot tolerate them, only if they have: 1.1. peripheral arthritis with 3 or more tender joints and 3 or more swollen joints **and** 1.2. moderate to severe psoriasis (a body surface area of at least 3% affected by plaque psoriasis and a Psoriasis Area and Severity Index [PASI] score greater than 10) **and** 1.3. had 2 conventional DMARDs and at least 1 biological DMARD. 1.4. Guselkumab is recommended only if the company provides it according to the commercial arrangement. 2. Assess the response to guselkumab from 16 weeks. Stop guselkumab at 24 weeks if psoriatic arthritis has not responded adequately using the Psoriatic Arthritis Response Criteria (PsARC; an adequate response is an improvement in at least 2 of the 4 criteria, 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria). If PsARC response does not justify continuing treatment but there is a PASI 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response. 3. Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the PsARC, and make any appropriate adjustments.

4. Take into account how skin colour could affect the PASI score, and make any appropriate adjustments.
5. These recommendations are not intended to affect treatment with guselkumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.