Northamptonshire County-wide commissioning guidance on High-cost biological & targeted synthetic Disease Modifying Anti-Rheumatic Drug (DMARD) therapies for the Treatment of Psoriatic Arthritis (PsA)

Northamptonshire Clinical Commissioning Groups (CCG) commission the use of high-cost DMARD therapies for PsA. This guidance is based on NICE and locally agreed guidance for the use of specialist drug therapy in the management of PsA.

The guidance is intended to cover initiation or change of treatment with a biological DMARD (bDMARD) or targeted synthetic DMARD (ts-DMARD) in patients with PsA or peripheral joint predominant Spondyloarthritis (SpA)

- A new Blueteq request is required
- Any deviations from this guidance will require prior approval by Northamptonshire CCG

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis characterised by pain, swelling and stiffness in and around the joints, often co-presenting with psoriasis. It is a type of inflammatory arthritis which can also affect the joints of the spine and therefore it is classified as a Spondyloarthritis (SpA). Both PsA and psoriasis are autoimmune long-term conditions that currently have no cure. Occasionally patients with SpA present with predominantly peripheral joint involvement and little spinal involvement and NICE suggests following the PsA guidance and not the Axial Spondyloarthritis (AxSpA) guidelines; these conditions include the enteropathic arthritis group (Crohn's or Ulcerative Colitis related arthritis) and the Chronic Reactive Arthritis Group. [1]

These therapies are only available for Specialist prescribing **ONLY**.

NICE has published a number of technology appraisals on the management of active PsA which has failed to respond to standard therapy (Table 1). For peripheral joint involvement active disease is defined as ≥ 3 tender and swollen joints, having failed 2 × systemic oral DMARDs, one of which must be Methotrexate (unless contra-indicated). There are further new treatments currently being appraised by NICE e.g. Upadacitinib and Guselkumab. [1]

For spinal disease involvement the criteria used are those for AxSpA and non-radiographic AxSpA (nrAxSpA) where active disease is a BASDAI[ϖ] > 4 and Spinal pain VAS[ϖ] >4 and the patient has failed 2 x NSAIDs[ϖ] at full dose.

As stipulated in the RMOC advisory statement (updated May 2020) on sequential use of biologic medicines, **prescribing choice of high-cost drug should be made on grounds of clinical and cost-effectiveness, and ensuring that the most appropriate and safe treatment option is selected through shared decision-making.**[2] In some cases, it may be beneficial to decide appropriateness of further treatment options via a multidisciplinary team discussion. Where possible, the least expensive product, either biosimilar or originator should be prescribed. All DMARDs carry an increased risk of infection. Table 2 highlights specific circumstances where first line least expensive high-cost drug may not be appropriate. The treatment pathway is detailed in Page 3. [2]

[ϖ] BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; VAS = Visual Analogue Scale; NSAIDS = Non-steroidal anti-inflammatory drugs

A Treat-To-Target (T2T) approach is recommended where a treatment goal is agreed with the patient (either 1. Disease Remission or 2. Low Disease Activity) and treatment is adjusted depending on the results of frequent, regular disease activity assessments until the target is reached or a decision is made to alter the target (EULAR 2019).[3]

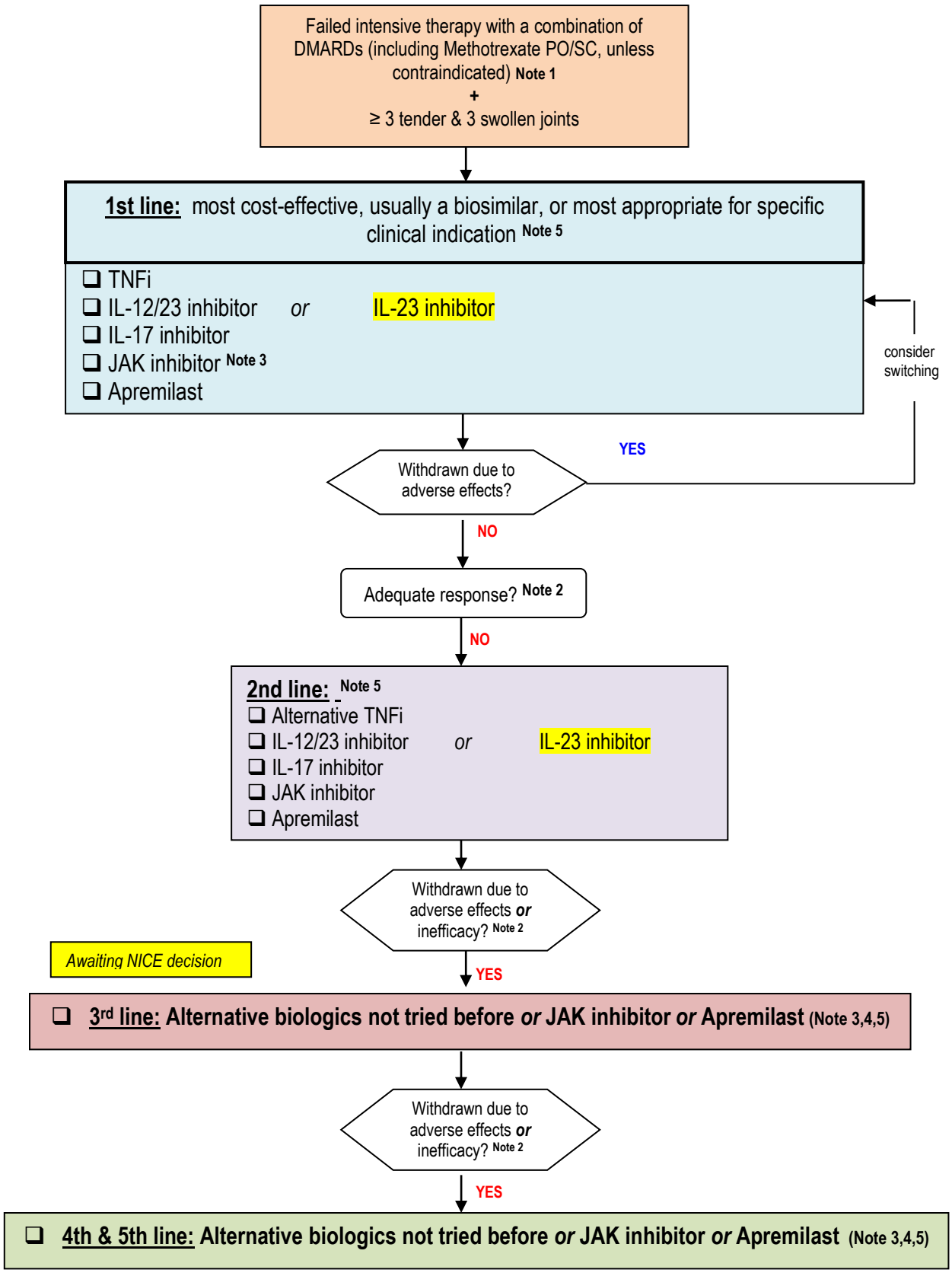
Table 1: NICE-approved bDMARDs and ts-DMARDs for use in PsA

bDMARD or ts DMARD	Class	Published date	NICE TAs	High-cost drugs	Additional Information
bDMARD	Anti-TNF inhibitor (TNFi)	25 August 2010	TA 199	Etanercept, Adalimumab & Infliximab	(i) TNFi agents for SC administration. (ii) Biosimilar products available. (iii) Infliximab can be administered as IV infusion
		27 April 2011	TA 220	Golimumab	(i) Most expensive SC TNFi (ii) 100mg dose for weight > 100kg
		24 May 2017	TA 445	Certolizumab	SC administration
	IL-12/23 inhibitor	4 June 2015 *(last updated 3 Mar 2017)*	TA 340	Ustekinumab	(i) SC administration every 12 weeks (ii) 90mg dose for weight > 100kg
	IL-23 inhibitor (IL-23i)	**Pending NICE FAD**		**Guselkumab**	**SC administration every 8 weeks**
	IL-17 inhibitor	24 May 2017	TA 445	Secukinumab	SC monthly administration with high-injection burden
		8 August 2018	TA 537	Ixekizumab	SC administration
tsDMARD	Phosphodiesterase-4 inhibitor (PDE-4i)	25 February 2017	TA 433	Apremilast	oral tablet
	Janus Kinase Inhibitor (JAKi)	3 October 2018	TA 543	Tofacitinib	oral tablet co-prescribed with Methotrexate
		Pending NICE FAD		**Upadacitinib**	**oral tablet**

Tablet 2: List of Patient Characteristics and preferred treatment option

Patient Characteristic	Drug Choice
Diverticulitis	Avoid JAKi
High-risk of thrombosis	Avoid JAKi
Inflammatory bowel disease	Adalimumab, Infliximab, Ustekinumab, Tofacitinib
Needle-phobia	Oral agents or biologics with less frequent dosing e.g. Ustekinumab, Ixekizumab
Psoriasis	Apremilast, Adalimumab, Etanercept, Infliximab (particularly nail psoriasis), Ixekizumab, Secukinumab, Ustekinumab
Spinal predominant disease	Follow Ankylosing spondylitis pathways (AxSpA or nr-AxSpA)
Uveitis	Adalimumab, Infliximab
Women of child-bearing age	Certolizumab (can be used throughout pregnancy & lactation), Etanercept & Adalimumab (can be used in 1st & 2nd trimester only) [4]

Biological & targeted synthetic DMARDs Pathway for Psoriatic Arthritis



1. A trial of DMARDs is defined as being normally of 6 months, with 2 months at standard dose, unless significant toxicity has limited the dose or duration of treatment.
2. Adequate response is defined as achieving improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC), one of which must be joint tenderness or swelling score, usually at 12 weeks following treatment initiation. 24 weeks if Ustekinumab; 16 weeks if Apremilast.
3. If inefficacy, consider trial of alternative biologics of different mode of action. Avoid cycling of TNFi if failed 2 x TNFis. Tofacitinib is to be co-prescribed with methotrexate
4. If adverse effects after progression through pathway, allow trials of any other NICE-approved biologics not tried before.
5. Discuss with patient for R&D if appropriate

References:

1. National Institute of Clinical Excellence (NICE TAs) www.nice.org.uk *<accessed 11th October 2020>*
2. Regional Medicines Optimisation Committee (RMOC) advisory statement on sequential use of biologic medicines (Updated May 2020) www.sps.nhs.uk *<accessed 12th October 2020>*
3. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update https://ard.bmj.com/content/79/6/700.1 *<accessed 12th October 2020>*
4. Flint J. Panchal S. et.al. British Society of Rheumatology (BSR) & British Health Professionals in Rheumatology (BHPR) guideline on prescribing drugs in pregnancy and breastfeeding – Part 1: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. *Rheumatology* 2016; **55**(9): 1693 – 1697 https://doi.org/10.1093/rheumatology/kev404

Appendix I: Individual Patient high-cost drugs therapy log

Affix addressograph here

1. Conventional systemic DMARDs treatment history

	csDMARDs tried	To continue with biologics? (✓/×)	Reason for stopping (ADR/CI)
1			
2			
3			
4			

2. Biologics/JAK treatment history (See Reference 1)

	Initiation Date	Drugs (specify brand if biosimilars available)	Reason for stopping/switching (Inefficacy / ADR/ other [please specify])
1			
2			
3			
4			
5			
6			

3. Document Disease Activity (PsARC)

	Date	TJC ≥ 3	SJC ≥ 3	Patient VAS (/5)	Physician VAS (/5)
1					
2					
3					
4					
5					
6					

Reference 1: Biologics/JAKs list (biosimilar brands highlighted in **bold**)

Mechanism of action	Biologics (originator brand)	Biosimilar available (✓/×)	Biosimilar Brands
TNFi	Adalimumab (Humira®)	✓	**Imraldi®** **Amgevita®**
	Certolizumab pegol (Cimzia®)	×	
	Etanercept (Enbrel®)	✓	**Benepali®** **Erelzi®**
	Golimumab (Simponi®)	×	
	Infliximab (Remicade®)	✓	**Remsima®**
IL-17 inhibitor	Ixekizumab (Taltz®) Secukinumab (Cosentyx®)	×	
IL-12/23 inhibitor	Ustekinumab (Stelara®)	×	
IL-23 inhibitor	Guselkumab (Tremfya®)	×	
PDE4 inhibitor	Apremilast (Otezla®)	×	
JAK inhibitor	Tofacitinib (Xeljanz) *with Methotrexate* Upadacitinib (Rinvoq®)	× ×	