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EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update

Laure Gossec ,[1,2] Andreas Kerschbaumer ,[3] Ricardo J O Ferreira ,[4,5] Daniel Aletaha ,[3] Xenofon Baraliakos ,[6] Heidi Bertheussen,[7] Wolf-Henning Boehncke,[8] Bente Appel Esbensen ,[9,10] Iain B McInnes,[11] Dennis McGonagle,[12,13] Kevin L Winthrop ,[14] Andra Balanescu,[15] Peter V Balint,[16] Gerd R Burmester ,[17] Juan D Cañete ,[18,19] Pascal Claudepierre,[20,21] Lihi Eder ,[22] Merete Lund Hetland ,[23,24] Annamaria Iagnocco ,[25] Lars Erik Kristensen,[26,27] Rik Lories,[28,29] Rubén Queiro ,[30,31] Daniele Mauro ,[32] Helena Marzo-Ortega ,[12,13] Philip J Mease ,[33,34] Peter Nash ,[35] Wendy Wagenaar,[36,37] Laura Savage,[38] Georg Schett ,[39] Stephanie J W Shoop-Worrall ,[40] Yoshiya Tanaka ,[41] Filip E Van den Bosch ,[42] Annette van der Helm-van Mil,[43] Alen Zabotti ,[44] Désirée van der Heijde ,[43] Josef S Smolen[3]

Handling editor Dimitrios T Boumpas

For numbered affiliations see end of article.

Correspondence to
Laure Gossec, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Sorbonne Universite, Paris, France; laure.gossec@aphp.fr

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ABSTRACT

Objective New modes of action and more data on the efficacy and safety of existing drugs in psoriatic arthritis (PsA) required an update of the EULAR 2019 recommendations for the pharmacological treatment of PsA.

Methods Following EULAR standardised operating procedures, the process included a systematic literature review and a consensus meeting of 36 international experts in April 2023. Levels of evidence and grades of recommendations were determined.

Results The updated recommendations comprise 7 overarching principles and 11 recommendations, and provide a treatment strategy for pharmacological therapies. Non-steroidal anti-inflammatory drugs should be used in monotherapy only for mild PsA and in the short term; oral glucocorticoids are not recommended. In patients with peripheral arthritis, rapid initiation of conventional synthetic disease-modifying antirheumatic drugs is recommended and methotrexate preferred. If the treatment target is not achieved with this strategy, a biological disease-modifying antirheumatic drug (bDMARD) should be initiated, without preference among modes of action. Relevant skin psoriasis should orient towards bDMARDs targeting interleukin (IL)-23p40, IL-23p19, IL-17A and IL-17A/F inhibitors. In case of predominant axial or entheseal disease, an algorithm is also proposed. Use of Janus kinase inhibitors is proposed primarily after bDMARD failure, taking relevant risk factors into account, or in case bDMARDs are not an appropriate choice. Inflammatory bowel disease and uveitis, if present, should influence drug choices, with monoclonal tumour necrosis factor inhibitors proposed. Drug switches and tapering in sustained remission are also addressed.

Conclusion These updated recommendations integrate all currently available drugs in a practical and progressive approach, which will be helpful in the pharmacological management of PsA.

INTRODUCTION

Psoriatic arthritis (PsA) is a disease which has benefited from notable progress over recent years. Concepts have evolved, such as very early diagnosis and pre-PsA, as well as defining treatment targets and applying a holistic approach to comorbidity management.[1–4] Pharmacological options have extended, with the approval of new agents targeting various modes of action for PsA (as well as skin psoriasis). Drugs licensed for PsA now include (1) conventional synthetic (cs) disease-modifying antirheumatic drugs (DMARDs), such as methotrexate (MTX), sulfasalazine and leflunomide; (2) biological (b) DMARDs targeting tumour necrosis factor (TNF), the interleukin (IL)-12/23 or IL-23 pathway, and the IL-17A and IL-17A/F pathway; and (3) targeted synthetic (ts) DMARDs that inhibit Janus kinases (JAKs) or phosphodiesterase 4 (PDE4) (table 1).[5] New safety data have emerged in inflammatory arthritis, particularly a worldwide cautionary comment regarding JAK inhibitors (JAKis), following a large randomised controlled trial (RCT) of tofacitinib in rheumatoid arthritis (RA).[6–8] Since the last EULAR recommendations for the pharmacological management of PsA in 2019, the field has changed significantly.[9–12] An update of the EULAR PsA management recommendations was therefore timely.[9]

This update addresses the non-topical, pharmacological management of PsA, with a specific focus on musculoskeletal (MSK) manifestations, while also addressing the spectrum of PsA, including how skin psoriasis, extra-MSK manifestations and comorbidities should influence treatment choices.

METHODS

In accordance with the EULAR updated standardised operating procedures,[13] the process

Table 1 Disease-modifying treatment options for psoriatic arthritis in 2023

Type of DMARD	Target	Name of drug
csDMARD		► Methotrexate ► Leflunomide ► Sulfasalazine
bDMARD	TNF	► Adalimumab ► Certolizumab ► Etanercept ► Infliximab ► Golimumab
	IL-12/23	► Ustekinumab
	IL-17A	► Ixekizumab ► Secukinumab
	IL-17A/F	► Bimekizumab
	IL-23-p19	► Guselkumab ► Risankizumab
	CTLA4	► Abatacept
tsDMARD	PDE4	► Apremilast
	JAK	► Tofacitinib. ► Upadacitinib.

Drugs currently authorised as of December 2023 for use in psoriatic arthritis.
bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug; IL, interleukin; JAK, Janus kinase; PDE4, phosphodiesterase 4; TNF, tumour necrosis factor; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

leading to this update included a data-driven approach and expert opinion.

After approval for an update by the EULAR Council in September 2022, taskforce members were selected by the convenor (JSS) and the methodologist (LG), to include more than one-third of new members, as well as country and gender representation. For the first time, experts from Australia, Japan and North America participated. Representatives from the health professionals in rheumatology (HPR) committee, patient research partners from PARE (People with Arthritis/Rheumatism) and young colleagues from the EMEUNET (EMerging EUlar NETwork) were included. Five members were recruited through an open call to EULAR countries via a competitive application process.

In October 2022, the steering group had its first meeting. The steering group consisted of seven rheumatologists (including the convenor, the methodologist and the fellow: JSS, LG, AK, DA, XB, IBM and DGM), a dermatologist (W-HB), an infectious disease specialist (KLW), an experienced fellow rheumatologist (AK), a patient research partner (HB) and two health professionals (BAE and RJOF, the latter acting in the capacity of a junior methodologist). Questions were then defined and addressed through a systematic literature review (SLR), performed by the fellow (AK) between November 2022 and April 2023, for the literature pertaining to pharmacological treatments of PsA and published since the previous SLR (ie, since the end of 2018).[5]

The taskforce comprised the steering group and 23 other experts; members came from 19 different countries (of which 15 were EULAR countries), and included 27 rheumatology specialists, 2 dermatologists, 1 infectious disease specialist, 2 people affected with PsA acting as patient research partners, 2 HPRs and 3 rheumatology/epidemiology fellows/trainees. Overall, 47% of the taskforce members had not participated in the previous update in 2019. In April 2023, the taskforce met for a physical meeting to develop the updated bullet points. Each point was discussed in detail both in smaller (breakout) groups and in plenary sessions until consensus was reached. Group approval was sought through votes (by raised hands) for each bullet point; the limit for acceptance of individual recommendations was set at ≥75% majority among the taskforce for the first voting round; then (after discussions and potential reformulations) at ≥67% majority; and finally, if required, the last round of votes was accepted with >50% acceptance or else a proposal was rejected.[13]

Although the SLR was a strong component of the discussions, the process was not only evidence-based but also experience-based and consensus-based, and included consideration of safety, efficacy, cost and long-term data. The levels of evidence (LoE) and grades of recommendation (GoR) were determined for each recommendation based on the Oxford Evidence Based System.[13 14] In May 2023, an anonymised email-based voting on the level of agreement (LoA) among the taskforce members was performed on a 0–10 scale (with 10 meaning full agreement) allowing calculation of mean LoA.

RESULTS

These recommendations address non-topical pharmacological treatments with a main focus on MSK manifestations. These recommendations concern stakeholders, such as experts involved in the care of patients with PsA, particularly rheumatologists and other health professionals (such as rheumatology nurses), general practitioners, dermatologists and other specialists; and also people with PsA as well as other stakeholders, for example, government and hospital officials, patient organisations, regulatory agencies and reimbursement institutions.

The overarching principles (OAPs) and recommendations are shown in table 2, with LoE, GoR and LoA. The updated recommendations include 7 OAPs (vs 6 in 2019) and 11 recommendations (vs 12 in 2019, due to merges). Of the 11 recommendations, only 4 are unchanged compared with 2019 (the modifications compared with the 2019 recommendations are represented in table 3).

Overarching principles

Of the seven OAPs, three remain unchanged, three were reworded and one has been added (overarching principle G). For more information on the thought process leading to the OAPs (unchanged or slightly changed), please refer to the 2015 and 2019 recommendations manuscripts.[9 15] Key points from the discussion of the OAPs are addressed in the following:

A. Psoriatic arthritis is a heterogeneous and potentially severe disease, which may require multidisciplinary treatment (unchanged).

Although PsA is potentially severe, not all patients will develop severe forms.[16 17] Multidisciplinary management is helpful for many patients, through collaboration between physicians of different specialties and HPRs with the appropriate expertise.[18 19]

B. Treatment of psoriatic arthritis patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist, considering efficacy, safety, patient preferences and costs.

This OAP was modified from 2019 to add patient preferences as an element to be considered and emphasise the importance of shared decision-making to maximise treatment adherence and efficacy while at the same time minimise complications driven by uncontrolled (active) disease as well as potential side effects of pharmacological drugs.[20 21]

Table 2 2023 updated EULAR recommendations for the pharmacological management of psoriatic arthritis

	Overarching principles			Level of agreement, mean (SD)
A	Psoriatic arthritis is a heterogeneous and potentially severe disease, which may require multidisciplinary treatment.			10.0 (0.1)
B	Treatment of psoriatic arthritis patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist, considering efficacy, safety, patient preferences and costs.			9.7 (0.6)
C	Rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with psoriatic arthritis; in the presence of clinically relevant skin involvement, a rheumatologist and a dermatologist should collaborate in diagnosis and management.			9.7 (0.5)
D	The primary goal of treating patients with psoriatic arthritis is to maximise health-related quality of life, through control of symptoms, prevention of structural damage, normalisation of function and social participation; abrogation of inflammation is an important component to achieve these goals.			9.9 (0.3)
E	In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly.			9.8 (0.4)
F	When managing patients with psoriatic arthritis, non-musculoskeletal manifestations (particularly skin, eye and gastrointestinal tract) should be taken into account; comorbidities such as obesity, metabolic syndrome, cardiovascular disease or depression should also be considered.			9.7 (0.7)
G	The choice of treatment should take account of safety considerations regarding individual modes of action to optimise the benefit–risk profile.			9.9 (0.4)
	Recommendations	**Level of evidence**	**Grade of recommendation**	**Level of agreement, mean (SD)**
1	Treatment should be aimed at reaching the target of remission or, alternatively, low disease activity, by regular disease activity assessment and appropriate adjustment of therapy.	1b	A	9.5 (1.0)
2	Non-steroidal anti-inflammatory drugs may be used to relieve musculoskeletal signs and symptoms[a]; local injections of glucocorticoids may be considered as adjunctive therapy[b].	1b[a], 3b[b]	A[a], C[b]	9.5 (0.7)
3	In patients with polyarthritis, or those with monoarthritis/oligoarthritis and poor prognostic factors[a] (eg, structural damage, elevated acute phase reactants, dactylitis or nail involvement), a csDMARD should be initiated rapidly, with methotrexate preferred in those with clinically relevant skin involvement.	1b, 4[a]	B, C[a]	9.3 (0.8)
4	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced.	1a	A	9.5 (1.3)
5	In patients with peripheral arthritis and an inadequate response to at least one bDMARD, or when a bDMARD is not appropriate[a], a JAKi may be considered, taking safety considerations* into account.	1b, 4[a]	B, D[a]	9.1 (1.5)
6	In patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAKi* is appropriate, a PDE4 inhibitor may be considered.	1b	B	8.7 (1.1)
7	In patients with unequivocal enthesitis and an insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered.	1b	B	9.5 (0.9)
8	In patients with clinically relevant axial disease with an insufficient response to NSAIDs, therapy with an IL-17A inhibitor, a TNF inhibitor, an IL-17 A/F inhibitor or a JAKi* should be considered.	1b	B	9.4 (1.3)
9	The choice of the mode of action should reflect non-musculoskeletal manifestations related to psoriatic arthritis; with clinically relevant skin involvement, preference should be given to an IL-17A or IL-17A/F or IL-23 or IL-12/23 inhibitor; with uveitis to an anti-TNF monoclonal antibody; and with IBD to an anti-TNF monoclonal antibody or an IL-23 inhibitor or IL-12/23 inhibitor or a JAKi*.	1b	B	9.6 (0.7)
10	In patients with an inadequate response or intolerance to a bDMARD or a JAKi, switching to another bDMARD or JAKi* should be considered[a], including one switch within a class[b].	1b[a], 4[b]	C	9.5 (0.7)
11	In patients in sustained remission, tapering of DMARDs may be considered.	2b	B	9.4 (1.2)

'Mild disease' is defined as oligoarticular or entheseal disease without poor prognostic factors and limited skin involvement.
csDMARDs (conventional synthetic DMARDs) include methotrexate, sulfasalazine or leflunomide. bDMARDs (biologic DMARDs) here include TNF inhibitors (both original and biosimilars), drugs targeting the IL-17 and IL-12–23/IL-23-p19 pathways, and in the context of recommendation 10 also CTLA4 (cytotoxic T-lymphocyte–associated antigen 4) inhibition. JAKis (Januse kinase inhibitors) include tofacitinib and upadacitinib.
The superscript letters 'a' and 'b' are used to link a part of the recommendation to a level of evidence.
The table shows the level of evidence, grade of recommendation and level of agreement among taskforce members (0–10 scale).
*For JAKis, caution is needed for patients aged 65 years or above, those who are current or past long-time smokers, with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors or with other malignancy risk factors, and with known risk factors for venous thromboembolism.
bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; CTLA4, cytotoxic T-lymphocyte–associated antigen 4; DMARDs, disease-modifying antirheumatic drugs; IBD, inflammatory bowel disease; IL, interleukin; JAKi, Janus kinase inhibitor; NSAIDs, non-steroidal anti-inflammatory drugs; PDE4, phosphodiesterase 4; TNF, tumour necrosis factor.

C. Rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with psoriatic arthritis; in the presence of clinically relevant skin involvement, a rheumatologist and a dermatologist should collaborate in diagnosis and management.

We consider that rheumatology experts provide the best care for patients with PsA, given their experience with the many drugs used to treat these and other rheumatic and musculoskeletal diseases (RMDs), including the important aspects of safety and comorbidities. Consultation with dermatologists and sometimes other specialists may be helpful in individual clinical scenarios (see also overarching principles F and G). A very slight rewording was performed to discuss skin involvement as 'clinically relevant' rather than 'clinically significant' for more homogeneity with other bullet points. This bullet point does not address the role of HPRs, who are usually not prescribers in EULAR countries.

Table 3 Comparison of the 2019 and 2023 EULAR recommendations for the management of psoriatic arthritis

2019 version		Changes performed	2023 version	
Overarching principles				
A	Psoriatic arthritis is a heterogeneous and potentially severe disease, which may require multidisciplinary treatment.	Unchanged	A	Psoriatic arthritis is a heterogeneous and potentially severe disease, which may require multidisciplinary treatment.
B	Treatment of psoriatic arthritis patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist, considering efficacy, safety and costs.	Reformulated	B	Treatment of psoriatic arthritis patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist, considering efficacy, safety, *patient preferences* and costs.
C	Rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with psoriatic arthritis; in the presence of clinically significant skin involvement, a rheumatologist and a dermatologist should collaborate in diagnosis and management.	Reformulated	C	Rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with psoriatic arthritis; in the presence of clinically *relevant* skin involvement, a rheumatologist and a dermatologist should collaborate in diagnosis and management.
D	The primary goal of treating patients with psoriatic arthritis is to maximise health-related quality of life, through control of symptoms, prevention of structural damage, normalisation of function and social participation; abrogation of inflammation is an important component to achieve these goals.	Unchanged	D	The primary goal of treating patients with psoriatic arthritis is to maximise health-related quality of life, through control of symptoms, prevention of structural damage, normalisation of function and social participation; abrogation of inflammation is an important component to achieve these goals.
E	In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly.	Unchanged	E	In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly.
F	When managing patients with psoriatic arthritis, non-musculoskeletal manifestations (skin, eye and gastrointestinal tract) should be taken into account; comorbidities such as metabolic syndrome, cardiovascular disease or depression should also be considered.	Reformulated	F	When managing patients with psoriatic arthritis, non-musculoskeletal manifestations (particularly skin, eye and gastrointestinal tract) should be taken into account; comorbidities such as *obesity*, metabolic syndrome, cardiovascular disease or depression should also be considered.
		New	G	The choice of treatment should take account of safety considerations regarding individual modes of action to optimise the benefit–risk profile.
Recommendations				
1	Treatment should be aimed at reaching the target of remission or, alternatively, low disease activity, by regular disease activity assessment and appropriate adjustment of therapy.	Unchanged	1	Treatment should be aimed at reaching the target of remission or, alternatively, minimal/low disease activity, by regular monitoring and appropriate adjustment of therapy.
2 and 3	Non-steroidal anti-inflammatory drugs may be used to relieve musculoskeletal signs and symptoms. Local injections of glucocorticoids should be considered as adjunctive therapy in psoriatic arthritis; systemic glucocorticoids may be used with caution at the lowest effective dose.	*Merged and modified*	2	Non-steroidal anti-inflammatory drugs may be used to relieve musculoskeletal signs and symptoms; local injections of glucocorticoids may be considered as adjunctive therapy.
4 and 5	In patients with polyarthritis, a csDMARD should be initiated rapidly, with methotrexate preferred in those with relevant skin involvement. In patients with monoarthritis or oligoarthritis, particularly with poor prognostic factors such as structural damage, high erythrocyte sedimentation rate / C-reactive protein, dactylitis or nail involvement, a csDMARD should be considered.	*Merged and modified*	3	In patients with polyarthritis, or those with monoarthritis/ oligoarthritis and poor prognostic factors (eg, structural damage, elevated acute phase reactants, dactylitis or nail involvement), a csDMARD should be initiated rapidly, with methotrexate preferred in those with clinically relevant skin involvement.
6	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced; when there is relevant skin involvement, an IL-17 inhibitor or IL-12/23 inhibitor may be preferred.	*Split into two recommendations*	4	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced.
7	In patients with peripheral arthritis and an inadequate response to at least one csDMARD and at least one bDMARD, or when a bDMARD is not appropriate, a JAK inhibitor may be considered.	*Modified*	5	In patients with peripheral arthritis and an inadequate response to at least one bDMARD, or when a bDMARD is not appropriate, a JAKi may be considered, taking safety considerations into account.
8	In patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAK inhibitor is appropriate, a PDE4 inhibitor may be considered.	Unchanged	6	In patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAKi is appropriate, a PDE4 inhibitor may be considered.
9	In patients with unequivocal enthesitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered.	Unchanged	7	In patients with unequivocal enthesitis and an insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered.
10	In patients with predominantly axial disease which is active and has insufficient response to NSAIDs, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor; when there is relevant skin involvement, IL-17 inhibitor may be preferred.	*Modified*	8	In patients with clinically relevant axial disease with an insufficient response to NSAIDs, therapy with an IL-17Ai, a TNFi, an IL-17 A/Fi or a JAKi should be considered.

Continued

Table 3 Continued

2019 version		Changes performed	2023 version	
		New	9	The choice of the mode of action should reflect non-musculoskeletal manifestations related to psoriatic arthritis; with clinically relevant skin involvement, preference should be given to an IL-17A or IL-17A/F or IL-23 or IL-12/23 inhibitor; with uveitis to an anti-TNF monoclonal antibody; and with IBD to an anti-TNF monoclonal antibody or an IL-23i or IL-12/23i or a JAKi.
11	In patients who fail to respond adequately to or are intolerant of a bDMARD, switching to another bDMARD or tsDMARD should be considered, including one switch within a class.	*Modified*	10	In patients with an inadequate response or intolerance to a bDMARD or a JAKi, switching to another bDMARD or JAKi should be considered, including one switch within a class.
12	In patients in sustained remission, cautious tapering of DMARDs may be considered.	Reformulated	11	In patients in sustained remission, tapering of DMARDs may be considered.

bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug; IBD, inflammatory bowel disease; IL, interleukin; JAK, Janus kinase; JAKi, Janus kinase inhibitor; NSAID, non-steroidal anti-inflammatory drug; PDE4, phosphodiesterase 4; TNF, tumour necrosis factor; TNFi, tumour necrosis factor inhibitor; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

D. The primary goal of treating patients with psoriatic arthritis is to maximise health-related quality of life, through control of symptoms, prevention of structural damage, normalisation of function and social participation; abrogation of inflammation is an important component to achieve these goals (unchanged).

For more details, please see the 2019 update of these recommendations.[9]

E. In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly (unchanged).

For more details, please refer to the 2019 update.[9]

F. When managing patients with psoriatic arthritis, non-musculoskeletal manifestations (skin, eye and gastrointestinal tract) should be taken into account; comorbidities such as obesity, metabolic syndrome, cardiovascular disease or depression should also be considered.

The wording 'such as obesity' was added, since obesity is frequent in PsA and can influence outcomes.[22 23] Obesity concerns excess body fat, while metabolic syndrome is a collection of risk factors that increase the likelihood of developing cardiovascular disease and type 2 diabetes. Obesity is a significant contributor to the development of metabolic syndrome. The taskforce members discussed if other comorbidities should be added, but it was felt that the term 'such as' entails that comorbidities overall should be considered, without a need to list them. Depression and potentially other mental health issues may influence treatment choice. Central sensitisation to pain perception is frequent in PsA and also influences outcomes; this may lead to difficulties in disease management.[24 25] Bone health and malignancies were also specifically highlighted. The management of comorbidities poses specific issues, in particular as to who is responsible for managing distinct disease domains. Solutions need to be applied according to the individual patient, each country's specific setting and healthcare system organisation.

G. The choice of treatment should take account of safety considerations regarding individual modes of action to optimise the benefit–risk profile (new).

Given new data on the safety of different modes of action, the taskforce proposed this new OAP to emphasise the importance of taking into account safety considerations for each patient.[6] The taskforce was aware that this item is somewhat redundant with overarching principle B but wished to emphasise the importance of benefit–risk assessment when considering the use of specific agents.

Recommendations

Of note, these recommendations are centred on non-topical pharmacological treatments; topical and non-pharmacological treatments are also important in PsA but are outside our scope. Figure 1 shows a summarised algorithm of the treatment proposals.

Some safety issues will be briefly addressed, but for a full picture of the adverse event profile of different drugs the package inserts should be consulted.

Recommendation 1

Treatment should be aimed at reaching the target of remission or, alternatively, low disease activity, by regular disease activity assessment and appropriate adjustment of therapy.

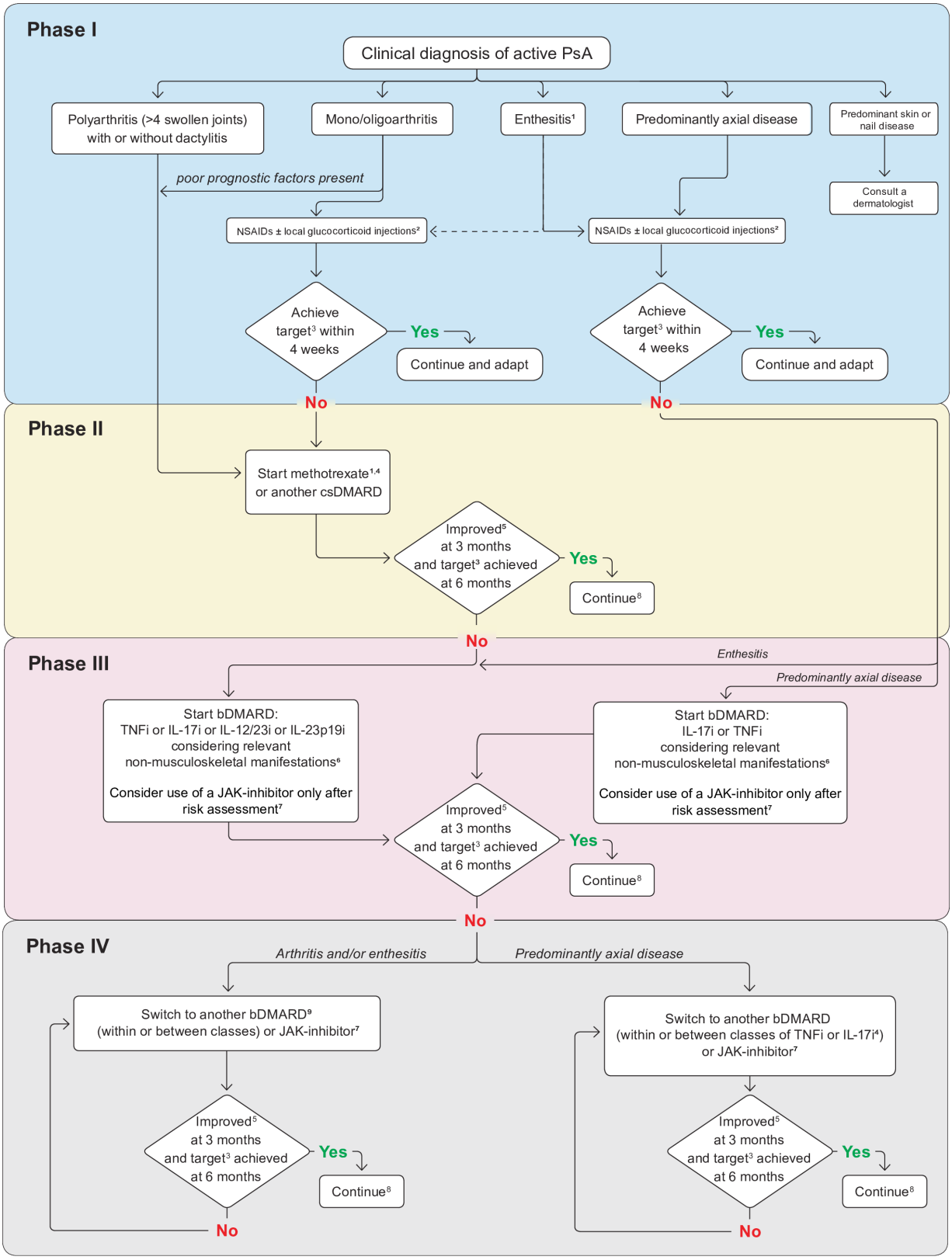
This (unchanged) recommendation is in keeping with the principles of treating-to-target.[26 27] Given the lack of new data to support treat-to-target in PsA, the LoE and GoR are also unchanged. The use of instruments to assess disease activity has been addressed in the treat-to-target recommendations.[26] The definition of remission in PsA remains a subject of debate.[28–30] For the context of these recommendations, remission should be seen as an abrogation of inflammation.

The taskforce members emphasised that disease activity should be regularly assessed across individual involved manifestations (eg, joints, skin, enthesitis, dactylitis, axial disease), and that treatment adjustments will depend on the predominant manifestation of the disease at a given moment.[31]

Recommendation 2

Non-steroidal anti-inflammatory drugs may be used to relieve musculoskeletal signs and symptoms; local injections of glucocorticoids may be considered as adjunctive therapy.

This recommendation deals with the short-term use of symptomatic treatment. It was developed by merging the two previous recommendations 2 and 3, which dealt separately with non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids, as both only serve to relieve symptoms in the short term. It was decided to no longer allude to systemic glucocorticoids in a bullet point, since the data underlying the prescription of systemic glucocorticoids in PsA are scarce. Moreover, glucocorticoids harbour many potential safety issues, in particular when taking into account the high prevalence of comorbidities and cardiovascular risk factors in PsA.[3 32] However, the taskforce members agreed that, in some selected cases, systemic glucocorticoid therapy may be helpful for some patients, especially for polyarticular forms and/or as bridging therapy.



1. *Some studies suggest that enthesitis may respond to methotrexate, but the level of evidence is low.*
2. *No glucocorticoids for axial disease.*
3. *The target is remission or low disease activity (especially with long standing disease) in accordance with the treat-to-target recommendations.*
4. *Preferred in the presence of relevant skin involvement, however in case of concomitant inflammatory bowel disease or uveitis, a TNF monoclonal antibody or (for IBD) IL-23i or 12/23i or JAKi is recommended.*
5. *Improvement means at least 50% reduction in disease activity.*
6. *Arthritis/enthesitis: TNFi or IL-17i or IL-12/23i or IL-23p19i; Skin: IL-17i or IL-12/23i or IL-23p19i; Uveitis: anti-TNF monoclonal antibody; IBD: anti-TNF monoclonal antibody or IL-12/23i or IL-23p19i or JAKi; Consider using PDE4i in mild disease if bDMARD and JAKi is inappropriate.*
7. *For JAK-inhibitors, caution is needed for patients aged 65 years or above, current or past long-time smokers, with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors or with other malignancy risk factors; with known risk factors for venous thromboembolism.*
8. *Consider tapering in sustained remission.*
9. *Including abatacept.*

Figure 1 2023 EULAR recommendations algorithm for the management of PsA. bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IBD, inflammatory bowel disease; L, interleukin; JAK, Janus kinase inhibitor; JAKi, Janus kinase inhibitor; NSAID, non-steroidal anti-inflammatory drugs; TNF, tumour necrosis factor; TNFI, tumour necrosis factor inhibitor.

NSAIDs offer symptomatic relief to patients with MSK involvement, but have not shown any efficacy in psoriasis. NSAIDs and local glucocorticoid injections are useful to relieve symptoms and local inflammation temporarily, and may be used combined with DMARDs as needed (please see recommendation 3). However, the safety aspects of (potentially long-term) NSAID use have to be taken into account.

The taskforce emphasised that the vast majority of patients should not be treated with NSAIDs alone (without DMARDs), in keeping with a proactive treat-to-target approach to PsA. Only patients with very mild peripheral disease, or with predominant entheseal or axial disease, may sufficiently benefit from NSAIDs as monotherapy. Even in these cases, it is proposed that the use of symptomatic treatments alone should usually be short term, for example, limited to 4 weeks or so. In peripheral arthritis, this duration is based on the opinion of the group; in predominant axial disease, it is in keeping with the Assesment of Spondyloarthritis International Society (ASAS)/EULAR recommendations for axial spondyloarthritis (axSpA) whereby persistent disease after 4 weeks of treatment is considered a failure of NSAIDs.[33] On the other hand, for patients with predominant axial disease who experience significant improvement in clinical symptoms, continuous NSAID use may be proposed if needed to control symptoms, always taking the risks and benefits into account. Of note, data regarding the efficacy of NSAIDs in enthesitis are limited.

Recommendation 3

In patients with polyarthritis or those with monoarthritis/oligoarthritis and poor prognostic factors (eg, structural damage, elevated acute phase reactants, dactylitis or nail involvement), a csDMARD should be initiated rapidly, with methotrexate preferred in those with clinically relevant skin involvement.

Among patients with peripheral arthritis,[34 35] a distinction is made according to the number of swollen joints and according to prognostic factors.[36] In 2019, polyarthritis and monoarthritis/oligoarthritis with poor prognostic markers were addressed in separate bullet points, which were merged for clarity in this update (table 3). Oligoarticular disease is defined as arthritis (swollen joints) of up to four (included) joints.[9] This definition applies to clinical detection (rather than imaging). The prognostic factors have also been previously defined[9 17] and are unchanged.

We recommend rapid csDMARD start, concomitant (or close) with the initiation of symptomatic therapy, for both patients with polyarticular disease and patients with oligoarticular disease and poor prognostic factors. Patients with oligoarticular disease and lack of poor prognostic factors should also receive a csDMARD, but there is less urgency for these patients given the more favourable long-term prognosis. The latter may receive csDMARDs after a longer delay, and potentially a period of symptomatic treatment alone (see recommendation 2). Since there is a lack of strong evidence to support this approach of rapid treatment introduction, this recommendation was mainly based on expert opinion.

Of note, there is no specific recommendation for dactylitis. We consider dactylitis as an association of (oligo)synovitis, tenosynovitis and enthesitis. Patients with isolated dactylitis should be treated similarly to patients with oligoarthritis; this includes the use of joint glucocorticoid injections and csDMARDs, which have shown efficacy in relieving dactylitis.[37]

The first DMARD should be a csDMARD (meaning MTX, leflunomide or sulfasalazine). The decision concerning the first-line DMARD is important and led to much taskforce discussion, and has been put as an element for further research in the research agenda (table 4). The continued prioritisation of csDMARDs reflects consensual expert opinion within the taskforce that favoured the benefit–risk–cost balance of csDMARDs and in particular MTX over targeted drugs. The absence of new data indicating the superiority of a b/tsDMARD as first-line, and

Table 4 Research agenda indicating priorities for future research in PsA

Theme	Question
Responsibility	► Role of the rheumatologist vs other specialists in the management of PsA.
Pathogenesis	► Pathogenesis of different tissue involvements in PsA. ► Pathogenesis of axial disease. ► Microbiome relationship to disease onset and progression. ► Prediction markers of response on synovial histopathology. ► Identification of new therapeutic targets. ► Understanding the biopathology of treatment-refractory PsA. ► Genetics of PsA.
Very early PsA	► Biomarkers for pre-PsA. ► Defining screening strategies for PsA among patients with psoriasis: is screening needed, and if so in which populations, how and when? ► Criteria for early diagnosis of PsA and role of imaging. ► Prevention of progression from psoriasis to PsA: pre-PsA therapy/interception (efficacy of DMARDs in preventing progression from Pso to PsA). ► Window of opportunity studies.
Drug ordering/response prediction and biomarkers	► Research on the effect of sex on treatment choices, treatment efficacy and treatment maintenance. ► Incorporating ultrasonography in decision-making. ► Biomarkers for prediction of disease and response. ► Prediction of response with genetics and polygenetics.
Prognosis	► Prognostic factors of progressive disease, structural damage and unfavourable functional outcomes. ► Predicting response to treatment (predicting response to NSAIDs, to csDMARDs, to the different bDMARDs, to tsDMARDs). ► Prognosis of early-onset (juvenile) PsA.
First DMARD choices	► Biosimilars vs methotrexate as first choice—strategy trials. ► Comparing direct and indirect costs, efficacy, side effects in employed, early, severe, bio-naïve PsA patient groups treated with methotrexate or biosimilars. Is there any advantage of using methotrexate over biosimilars in this group?
Outcomes in PsA	► Development/validation of composite scores of disease activity in PsA. ► Consensus on core outcomes in PsA trials. ► Coprimary outcomes for skin and joints. ► Efficacy of apremilast on structural changes. ► Drug-free remission as an outcome in PsA.
Treatments	► Efficacy of csDMARDs for dactylitis. ► Assessing combinations of csDMARDs with biologics compared with biologics monotherapy. ► Associations of bDMARDs.
Contextual factors in PsA	► Sex and gender. ► Age.
Safety	► Differential JAKi safety in PsA and across drugs. ► Tyrosine-kinase inhibition safety in PsA. ► Long-term safety trials in PsA.
Axial PsA	► Pathogenesis of axial PsA vs axSpA. ► Criteria for differentiation and overlap between axSpA and PsA. ► JAKis in axial PsA. ► Assessment of spinal disease: defining the similarities and differences with axSpA.
Comorbidities	► Impact of comorbidities on drug choice. ► Effect of metabolic intervention on disease activity. ► Effect of different DMARDs on cardiovascular risk. ► Influence of non-pharmacological interventions on multimorbidity. ► Entheseal PsA: overlap with widespread pain syndrome and role of imaging in the diagnosis. ► Treatment of pain which does not respond to usual therapies. ► Fatigue in PsA. ► Unravelling complexities of difficult-to-manage PsA.
Switches	► Repeat switching within a DMARD class. ► Switching and cycling between drugs.

axSpA, axial spondyloarthritis; bDMARDs, biological disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; DMARDs, disease-modifying antirheumatic drugs; JAKi, Janus kinase inhibitor; NSAIDs, non-steroidal anti-inflammatory drugs; PsA, psoriatic arthritis; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs.

in the presence of new data on MTX, was seen as confirming the efficacy of this drug in PsA.[5 37–39]

Since the EULAR recommendations adhere to a treat-to-target (T2T) approach which implies a reduction of disease activity by at least 50% within 3 months and reaching the treatment target within 6 months, a csDMARD should not be continued if these therapeutic goals are not attained. On csDMARD inefficacy, another DMARD, such as a bDMARD (see recommendation 4), can be rapidly instituted. Generally speaking, we recommend assessing the efficacy of the csDMARD and deciding if it should be pursued as monotherapy or not, after 12 weeks, in line with the T2T recommendations.[26] Although MTX use in PsA has typically been founded on evidence from other immune-mediated diseases such as RA and psoriasis,[40] there is also evidence for its efficacy in PsA, with recent confirmatory data both from observational data sources and from a randomised trial indicating that a proportion of patients will respond to escalation of doses of MTX.[39 41–43] The efficacy–safety balance of MTX should be assessed regularly, given the general metabolic profile of patients with PsA which can put them at a higher risk for adverse events such as hepatotoxicity.[42–44] The MTX dose should be sufficient, that is, usually between 20 mg and 25 mg weekly (about 0.3 mg/kg), and use of folate supplementation is recommended to reduce the adverse effects of MTX.[45]

Other csDMARDs (ie, leflunomide and sulfasalazine) are potential treatment options and have demonstrated efficacy in PsA peripheral arthritis.[15] A recent trial of the combination of MTX with leflunomide indicated a low efficacy to safety ratio; thus, this association is not recommended.[38]

Recommendation 4

In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced.

This recommendation is relevant to patients with peripheral arthritis and therefore is meant to include both those with monoarticular/oligoarticular and those with polyarticular disease. However, where peripheral involvement is limited and without poor prognostic factors, it is not unreasonable to apply a second csDMARD course before initiating a bDMARD/tsDMARD, when this decision is agreed by the prescriber and the patient.

After failure of at least one csDMARD, the taskforce proposed as next step one of the many available bDMARDs (table 1).[5]

JAKi is efficacious in PsA, but the taskforce decided that at present the efficacy–safety balance, costs and long-term experience with many bDMARDs clearly favour their recommendation over JAKi. Relevant comorbidities in many patients with PsA also favour bDMARD selection.

Regarding bDMARDs, no order of preference is given since no bDMARD has demonstrated superiority for joint involvement over other bDMARDs (table 1).[46–48] Herein they are listed in numeric order of the targeted cytokine, and not in order of preference. However, in the context of the present recommendation, CTLA4 (cytotoxic T-lymphocyte–associated antigen 4) inhibition is not considered a good option due to its limited efficacy in clinical trials.[49] The GoR is high for this bullet point, reflecting robust accrued data.[50]

Unlike MSK manifestations, non-MSK domains of PsA allow differential order of bDMARD recommendation (se recommendation 9).[5] Two head-to-head trials of bDMARDs in PsA, both comparing an IL-17A inhibitor with adalimumab, showed similar efficacy for IL-17A inhibition and TNF inhibition, as regards efficacy on the joints, while skin responses are better with the former.[46 47] We also note that there is evidence on the better efficacy of a bDMARD compared with MTX in skin psoriasis (and evidence for differences between bDMARDs, please see recommendation 9).[51 52]

All bDMARDs and JAKi showed efficacy regarding inhibition of radiographic progression; such data are lacking for apremilast.

The safety of the different available categories of bDMARDs appears acceptable in our SLR.[5] All bDMARDs increase the risk of infections.[5] The risks of TNF inhibitors (TNFis) are well known. Candidiasis (usually mucocutaneous) is more frequent with IL-17A and IL-17A/F inhibition, particularly the latter.[53 54] While IL-23-p19i is a more recent addition to the armament, its safety appears satisfactory, in line with ustekinumab which also interferes with IL-23 (p40 chain) whose adverse event profile is well known and appears satisfactory.[5]

As a general rule, safety and comorbidities need to be taken into account when a decision to start a new drug is taken. More complete information regarding the safety aspects of bDMARDs is provided in the individual drug's product information. Costs should also be taken into account, but these may vary at the country level; cost savings will occur in many countries due to the availability of biosimilar TNF blockers and potentially other biosimilars in due course. Personalised medicine, to facilitate an optimal choice of the first bDMARD, is currently difficult due to the lack of individualised predictors of response to treatment.[55] As previously discussed, it is of key importance to take into account the patient phenotype and potential extra-MSK features (figure 1). Comorbidities are also to be considered.[23 56] More research is needed on the predictors of drug response, including the effect of sex.[57 58]

Combination of a bDMARD with a csDMARD

First-line bDMARDs are often given in combination with csDMARDs, such as MTX.[41 59] However, there are conflicting data regarding the added benefit of concomitant MTX with targeted DMARDs in patients with peripheral disease and no evidence of a benefit of MTX in patients with axial symptoms.[33 60 61]

MTX combination with bDMARDs has been explored mainly for TNFi; studies have generally found similar efficacy with or without concomitant MTX, although with increased drug survival when using MTX, in some studies.[41 59 62] A recent large study reported increased remission rates with TNFi plus MTX combination therapy.[59] With other modes of action, there is a lack of data to support comedication. Overall, the taskforce proposed to combine a first bDMARD with the previously prescribed csDMARD, in all cases where such a treatment has already been tolerated by the patient and in particular when the first bDMARD is a TNFi. For other modes of action, given the lack of data, we cannot recommend comedication, although the usual practice would be to continue a csDMARD when initiating a bDMARD (doses of the csDMARD can be diminished if needed).

Recommendation 5

In patients with peripheral arthritis and an inadequate response to at least one bDMARD, or when a bDMARD is not appropriate, a JAKi may be considered, taking safety considerations into account.

This recommendation elicited much debate. On the one hand, since 2019, new data have accrued on JAKis in terms of efficacy, such as the publication of positive trials on upadacitinib in PsA.[63]

On the other hand, there is currently a worldwide cautionary statement issued by both the Food and Drug Administration and the European Medicine Agency restricting the use of JAKis in all diseases including PsA, based on an increased risk of cardiovascular and malignancy events observed with tofacitinib in older patients with RA with cardiovascular risk factors.[6–8] JAKis lead to increased general infection rates of similar magnitude to bDMARDs, but higher for herpes zoster infections.[5] Drug safety for the JAKis tofacitinib and upadacitinib in the specific context of PsA was recently reported and appeared reassuring; however, follow-up was short and further data are warranted.[64 65] While currently long-term extension data do not show increased cardiovascular/cancer risk related to JAKi use in PsA, there are no RCTs similar to the ORAL-Surveillance trial available at present in PsA. Therefore, the taskforce felt that the precautions related to RA also have to be taken for PsA, especially since various comorbidities important for the JAKi risk profile may be more prevalent in PsA than in RA (eg, obesity and cardiovascular risk factors). On the other hand, controlling inflammation is important to decrease cardiovascular risk.

Safety of JAKis should be carefully considered[66]; we propose in table 2 and figure 1 a shortened version of the EMA warning/limitation to use, which includes age, smoking status and other cardiovascular/venous/cancer risk factors.[7 8]

After much discussion, we considered that the efficacy–safety balance of JAKis did not justify putting JAKis on the same level as bDMARDs for order of choice (ie, proposing JAKis as usual treatment after insufficient response and/or intolerance to csDMARD treatment).

Therefore, JAKis are proposed usually as second-line targeted therapies (or third-line DMARDs). Of note, we recognise that, for some patients, JAKis may be a relevant option after a csDMARD; this is reflected in the wording of the bullet point ('when a bDMARD is not appropriate'). This 'non-appropriateness' may include contraindications to bDMARDs, practical issues leading to a strong preference for oral administrations (eg, lack of proper conservation at regulated temperatures) and patient preferences, including risk of non-adherence to injections (in accordance with the first OAP concerning shared decision-making). Nevertheless, patients will have to weigh their preferences against potential risks.

The GoR was low for this recommendation, in particular regarding safety considerations, since the data are sparse in PsA and we had to rely on data taken from RA. The taskforce suggests using JAKi after bDMARDs have failed because several new bDMARDs with excellent effects on skin involvement and relatively good safety data are now available (IL-23, IL-17 inhibitors) and more long-term data on JAKi efficacy and safety are needed in PsA. The efficacy to safety ratio of JAKis was also put into the research agenda (table 4).

Currently, drugs from the tyrosine kinase 2 (TYK2) pathway inhibition are being assessed in PsA[5]; they are not currently licensed for use, and indeed the data are at this point limited in particular for safety (including in psoriasis where such therapy is licensed). Thus, we did not include TYK2 inhibition in the current recommendations.

Recommendation 6

In patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAKi is appropriate, a PDE4 inhibitor may be considered.

This recommendation is unchanged from 2019, with unchanged LoE. 'Mild disease' is defined as oligoarticular or entheseal disease without poor prognostic factors and limited skin involvement.[9 67] The FOREMOST trial recently confirmed the efficacy of apremilast compared with placebo in oligoarticular PsA.[67] Nevertheless, the reason to place apremilast differently from bDMARDs or other tsDMARDs is not only based on its consistently relatively low efficacy, but also on the lack of structural efficacy data (thus putting the term 'DMARD' at risk since there are no data on inhibition of damage progression).

This recommendation received the lowest LoA within the taskforce, reflecting that more than a quarter of the taskforce participants were in favour of only discussing apremilast in the text without a specific bullet point.

The use of apremilast in combination with TNFi is off-label, and is a more costly drug combination with no supporting data and cannot be recommended.

Recommendation 7

In patients with unequivocal enthesitis and an insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered.

This bullet point remains unchanged. Unequivocal enthesitis refers (as in 2019) to definite entheseal inflammation (which might need additional diagnostic imaging) to avoid overtreatment of entheseal pain not related to PsA (eg, in the context of widespread pain syndrome or repetitive mechanical stress).[68 69] In terms of treatment options, the taskforce discussed the recent data indicating indirectly some efficacy for MTX in enthesitis.[5 38 39] However, it was felt that the data for MTX were not sufficiently strong to propose MTX in the bullet point. We do acknowledge that, for some patients with enthesitis, MTX may be an option (figure 1).

For unequivocal predominant enthesitis, the proposal is to introduce a bDMARD (without a preference for a specific mode of action) since all currently approved bDMARDs have demonstrated efficacy on enthesitis, with similar magnitudes of response, although head-to-head trials are missing (figure 1).[5] Here, costs may be important, but other manifestations will also have to be taken into account (see recommendations 8 and 9). Of note, although tsDMARDs are not mentioned specifically in the bullet point, they are an option in some cases of enthesitis (always considering benefit to risk ratios, in particular for JAKis).[7 8]

Recommendation 8

In patients with clinically relevant axial disease with an insufficient response to NSAIDs, therapy with an IL-17Ai, a TNFi, an IL-17 A/Fi or a JAKi should be considered.

The formulation for axial disease was modified from predominant to clinically relevant. For axial disease, in agreement also with the recently updated ASAS/EULAR axSpA recommendations,[33] we continue to judge csDMARDs as not relevant. bDMARDs targeting TNF and IL-17A and IL-17A/F as well as tsDMARDs targeting JAK are recommended. For JAKis, safety issues should be considered. Of note, we propose a choice between the drugs, not a combination of the drugs.

For this recommendation, the order of the drugs listed is of relevance, meaning that IL-17A inhibition has been put first due to the availability of currently only one trial specifically investigating axial PsA and using secukinumab (the MAXIMISE trial),[70] with the other drugs listed thereafter. Thus, the LoE is stronger for IL-17A inhibition than for the other drugs, where the data are derived from axial SpA.[33]

The other drugs are listed with TNF inhibition first due to long-term safety data, then IL-17 A/F inhibition which has been recently licensed for axial SpA and JAK inhibition as an option taking into account safety. JAKis are here proposed in the same recommendation as bDMARDs, also reflecting that comorbidity profiles of patients with predominant or isolated axial PsA may be more comparable to patients with axial SpA and therefore may have a more favourable safety profile with respect to cardiovascular and cancer risks than many patients with predominant peripheral arthritis. The taskforce discussed the circumstantial evidence that IL-23 inhibition may be efficacious for axial PsA; however, given negative trials for IL-12/23 inhibition in axSpA, the IL-23 pathway is not recommended here.[33 71–73] Axial PsA remains a challenging form of PsA in terms of definition and differences with axial SpA; thus, this phenotype is part of the research agenda (table 4).

Recommendation 9

The choice of the mode of action should reflect non-musculoskeletal manifestations related to PsA; with clinically relevant skin involvement, preference should be given to an IL-17A or IL-17A/F or IL-23 or IL-12/23 inhibitor; with uveitis to an anti-TNF monoclonal antibody; and with IBD to an anti-TNF monoclonal antibody or an IL-23 inhibitor or IL-12/23 inhibitor or a JAKi.

This is a new recommendation to clarify more visibly than in 2019 (table 3) that the choice of drug should take into account not only the MSK PsA phenotype but also extra-MSK manifestations.

The first extra-MSK manifestation of interest in PsA is skin psoriasis. Although most patients with PsA present with skin psoriasis or have a personal history of skin psoriasis, registry data indicate that many patients with PsA have mild skin involvement.[74] However, even limited skin psoriasis can be troublesome, since relevant skin involvement is defined as either extensive (body surface area involvement >10%), or as important to the patient, that is, impacting negatively their quality of life (such as is the case with face or genital involvement).[9] For these patients, we recommend preferentially considering drugs targeting the IL-17A, IL-17A/F or IL-23 pathway (here, the order between drugs is cited in order of numbered cytokine, not preference). There are strong data, including head-to-head trials, in the field of skin psoriasis showing that drugs targeting the IL-23 and IL-17 pathways are superior to TNFis and to JAKis for skin psoriasis.[51 52 75–78] This justified proposing these modes of action preferentially in case of relevant skin involvement. This is in keeping with psoriasis recommendations.[79]

Uveitis is not as frequent in PsA as it is in axial SpA; the prevalence is reported around 5%.[80] However, uveitis can be severe and should influence treatment decisions. Currently, the only mode of action with direct proof of efficacy on uveitis is TNF inhibition through monoclonal antibodies (ie, adalimumab and infliximab). Thus, for patients with uveitis, an anti-TNF monoclonal antibody is preferred.

Inflammatory bowel disease (IBD) concerns 2%–4% of patients with PsA.[80] The armamentarium for IBD has widened recently, and this recommendation reflects this fact, proposing that one of the modes of action currently licensed for IBD should be prescribed when it coexists with PsA. No order of preference is given here and prescribers are urged to adhere to EMA authorisations for IBD and take into account safety. For informative purposes, as of mid-2023, drugs authorised for IBD include anti-TNF monoclonal antibodies (ie, adalimumab and infliximab), the IL-12/23i ustekinumab, the IL-23i risankizumab (for Crohn's disease) and two JAKis (one of which, tofacitinib, only for Crohn's disease).[81–85] IL-17is (both A and A/F) are not recommended in case of active IBD, given indications of a heightened risk of flares.[86–88]

Decisions for patients presenting with major skin involvement, with uveitis or with IBD should be discussed with the relevant specialist colleagues, as needed.

In all cases, the prescriber must refer to current drug authorisations and take into account safety and comorbidities.

To present an order for choosing drugs, we propose that the first element to take into account is the PsA subtype, then as a second element extra-MSK manifestations (always considering safety and comorbidities).

Recommendation 10

In patients with an inadequate response or intolerance to a bDMARD or a JAKi, switching to another bDMARD or JAKi should be considered, including one switch within a class.

This recommendation is unchanged from 2019, with unchanged LoE.[9] After failing one targeted drug, it is logical to switch to another targeted drug; there are currently no strong data to prefer a switch with a change in mode of action to a switch within the same mode of action. Of note, this recommendation does not limit the total number of switches for a given patient. It also does not necessarily mean that more switches within a class could not be done, but the taskforce felt that a switch should not necessarily be done after one drug of a class has failed. Switches can be made, as appropriate, between bDMARDs, or between bDMARDs and JAKis. We include abatacept as a treatment option (table 1),[49] but note that it demonstrated modest efficacy and hence this is an option to be used only after failing one or more other targeted drugs. The efficacy of bimekizumab, the dual IL-17 A/F inhibitor, appeared similar in TNF-naïve and TNF-experienced populations; this will warrant confirmation.[53 54] Finally, a combination of bDMARDs is being explored, but cannot be recommended at this time.

Recommendation 11

In patients in sustained remission, tapering of DMARDs may be considered.

This bullet point is unchanged. However, more data have accrued on tapering, leading to a higher grade of recommendation.[89–91] By tapering we mean 'dose reduction' not drug discontinuation since the latter usually leads to flares. Drug tapering is a logical step when patients are doing well over time, from a safety and a cost perspective (tapering is often performed by the patient himself/herself alone). On the other hand, long-term data are missing and currently drug tapering is off-label. For all of these reasons, the taskforce kept the tentative wording of 'may be considered' (to ensure it is not made mandatory) and of course in the context of a shared decision with the patient (as is the case also for the other treatment decisions).

Research agenda

The taskforce felt that many issues needed more data, and an extensive research agenda was developed (table 4).

DISCUSSION

This paper presents updated recommendations for the management of PsA, a treatment algorithm and a research agenda. This update addresses all currently available drugs and modes of

action, and recommends an order to their use, taking into account the phenotype of the MSK and the non-MSK manifestations.

These elements should be helpful in the management of individual patients, but also in the advocacy for better access to care and for research.

This 2023 update is a major update since most of the recommendations were modified substantially. The EULAR standardised operating procedures propose a voting system for updates which discourages minor modifications for rewordings.[13] Since 2019, many new drugs have become available in PsA; the choice of which drug to prescribe to which patients rests on data related to efficacy, clinical phenotype, adverse event risk profile, tolerance, long-term data, cost and access. While laboratory biomarkers for stratified treatment approaches are lacking, the taskforce used clinical markers to develop clinical phenotypic preferences for specific drugs. In these updated recommendations, the taskforce applied expert opinion to the available data, to propose a pragmatic, logical order of a step-up approach to targeted treatments of PsA. The taskforce felt that proposing an order is helpful both for clinicians and to advocate for access to drugs for patients with PsA.

The drug options considered in these recommendations are currently licensed for PsA. We are aware that other drugs are being tested, or are available in other related conditions, especially skin psoriasis; however, these drugs are considered out of the scope of the present recommendations. Brodalumab was at the time of these recommendations only approved for psoriasis; TYK2 inhibitors such as deucravacitinib and brepocitinib have also been developed or in development for skin psoriasis and PsA; izokibep is a novel antibody mimetic, a small IL-17i currently undergoing testing; and an oral IL-23i is also in development.[5]

The taskforce had extensive discussions on the positioning of JAKi in the recommendations.[63 92] We as a group feel that it is important to *make haste slowly*, and to uphold high safety standards when promoting drugs with only short-to-medium-term experience and for which long-term data are lacking—not least in PsA. In fact, this cautious attitude was also adhered to in the 2019 recommendations, and further safety developments have later confirmed that this attitude was appropriate.[7 8] It is of key importance to continue monitoring the drugs and, ideally, perform controlled trials, as only hard and high-level data can be reassuring.

Costs are also an important aspect in patient management, and it is generally recommended to prescribe the cheaper drug if two agents have similar efficacy and safety. Of note, even if one mode of action may have somewhat better efficacy on certain manifestations, a less expensive agent could still be preferred as long as it does not bear much lesser efficacy in that disease domain. Biosimilars are available for several TNFis and have led to significant reduction in expenditure and more use in many countries, while their price is not much lower than that of originators in many other ones. Tofacitinib will soon become generic, and the same is true for apremilast, which should also lower the costs for these agents and allow wider application especially in less affluent countries. Thus, overall, the taskforce felt that the prescription of drugs would account for the relationships between efficacy, safety and cost, in line with the OAPs and the 11 recommendations which are summarised in the algorithm (figure 1). Many points are still to be confirmed in the management of PsA, leading to an extensive research agenda.[93]

In conclusion, the updated 2023 recommendations should be helpful to clinicians but also to health professionals and patients when discussing treatment options. They can also be helpful to promote access to optimal care. As new data become available and new drugs are authorised in PsA, these recommendations should be again updated.

Author affiliations
[1]INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Sorbonne Universite, Paris, France
[2]APHP, Rheumatology Department, Hopital Universitaire Pitie Salpetriere, Paris, France
[3]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria
[4]Nursing Research, Innovation and Development Centre of Lisbon (CIDNUR), Higher School of Nursing of Lisbon, Lisbon, Portugal
[5]Rheumatology Department, Centro Hospitalar e Universitário de Coimbra EPE, Coimbra, Portugal
[6]Rheumazentrum Ruhrgebiet, Ruhr University Bochum, Herne, Germany
[7]EULAR Patient Research Partner, EULAR, Oslo, Norway
[8]Dermatology and Venereology, Geneva University Hospitals, Geneva, Switzerland
[9]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet, Glostrup, Denmark
[10]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark
[11]College of Medical Veterinary and Life Sciences, University of Glasgow, Glasgow, UK
[12]LTHT, NIHR Leeds Biomedical Research Centre, Leeds, UK
[13]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK
[14]Division of Infectious Diseases, School of Medicine, School of Public Health, Oregon Health & Science University, Portland, Oregon, USA
[15]Sf Maria Hospital, University of Medicine and Pharmacy Carol Davila Bucharest, Bucharest, Romania
[16]Medical Imaging Centre, Semmelweis University, 3rd Rheumatology Department, National Institute of Musculoskeletal Diseases, Budapest, Hungary
[17]Department of Rheumatology and Clinical Immunology, Freie Universität Berlin and Humboldt-Universität zu Berlin, Charité Universitätsmedizin Berlin, Berlin, Germany
[18]Arthritis Unit, Department of Rheumatology, Hospital Clínic Barcelona, Barcelona, Spain
[19]FCRB, IDIBAPS, Barcelona, Spain
[20]Rheumatology, AP-HP, Henri Mondor University Hospital, Creteil, France
[21]EA Epiderme, UPEC, Creteil, France
[22]Department of Medicine, University of Toronto, Women's College Hospital, Toronto, Toronto, Canada
[23]The Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, Rigshospitalet Glostrup, Glostrup, Denmark
[24]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[25]Academic Rheumatology Centre, Dipartimento Scienze Cliniche Biologiche, Università di Torino - AO Mauriziano Torino, Turin, Italy
[26]The Parker Institute, Bispebjerg, Denmark
[27]Frederiksberg Hospital, Copenhagen University, Copenhagen, Denmark
[28]Laboratory of Tissue Homeostasis and Disease, Skeletal Biology and Engineering Research Center, KU Leuven, Leuven, Belgium
[29]Division of Rheumatology, University Hospitals Leuven, Leuven, Belgium
[30]Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain
[31]Translational Immunology Division, Biohealth Research Institute of the Principality of Asturias, Oviedo University School of Medicine, Oviedo, Spain
[32]Department of Precision Medicine, University of Campania Luigi Vanvitelli, Naples, Italy
[33]Rheumatology Research, Providence Swedish, Seattle, Washington, USA
[34]University of Washington School of Medicine, Seattle, Washington, USA
[35]School of Medicine, Griffith University, Brisbane, Queensland, Australia
[36]Tranzo, Tilburg School of Social and Behavioral Sciences, Tilburg University, Tilburg, The Netherlands
[37]Young PARE Patient Research Partner, EULAR, Zurich, Switzerland
[38]School of Medicine and Dermatology, Leeds Teaching Hospitals NHS Trust, University of Leeds, Leeds, UK
[39]Department of Internal Medicine 3, Rheumatology and Immunology and Universitätsklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany
[40]Children and Young Person's Rheumatology Research Programme, Centre for Musculoskeletal Research, The University of Manchester, Manchester, UK
[41]First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan
[42]Department of Internal Medicine and Pediatrics, VIB Center for Inflammation Research, Ghent University, Gent, Belgium
[43]Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

[44]Department of Medical and Biological Sciences, Azienda sanitaria universitaria Friuli Centrale, Udine, Italy

X Laure Gossec @LGossec, Ricardo J O Ferreira @FerreiraRJO, Lihi Eder @lihi_eder, Daniele Mauro @dranielmar, Peter Nash @drpnash and Stephanie J W Shoop-Worrall @sshoopworrall

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ORCID iDs
Laure Gossec http://orcid.org/0000-0002-4528-310X
Andreas Kerschbaumer http://orcid.org/0000-0002-6685-8873
Ricardo J O Ferreira http://orcid.org/0000-0002-2517-0247
Daniel Aletaha http://orcid.org/0000-0003-2108-0030
Xenofon Baraliakos http://orcid.org/0000-0002-9475-9362
Bente Appel Esbensen http://orcid.org/0000-0001-5331-8221
Kevin L Winthrop http://orcid.org/0000-0002-3892-6947
Gerd R Burmester http://orcid.org/0000-0001-7518-1131
Juan D Cañete http://orcid.org/0000-0003-2606-0573
Lihi Eder http://orcid.org/0000-0002-1473-1715
Merete Lund Hetland http://orcid.org/0000-0003-4229-6818
Annamaria Iagnocco http://orcid.org/0000-0001-5592-724X
Rubén Queiro http://orcid.org/0000-0002-8418-7145
Daniele Mauro http://orcid.org/0000-0002-9022-8863
Helena Marzo-Ortega http://orcid.org/0000-0002-9683-3407
Philip J Mease http://orcid.org/0000-0002-6620-0457
Peter Nash http://orcid.org/0000-0002-2571-788X
Georg Schett http://orcid.org/0000-0001-8740-9615
Stephanie J W Shoop-Worrall http://orcid.org/0000-0002-9441-5535
Yoshiya Tanaka http://orcid.org/0000-0002-0807-7139
Filip E Van den Bosch http://orcid.org/0000-0002-3561-5932
Alen Zabotti http://orcid.org/0000-0002-0573-464X
Désirée van der Heijde http://orcid.org/0000-0002-5781-158X

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