EuroGuiDerm Guideline for the systemic treatment of Psoriasis vulgaris

Overview of main recommendations and recommendations for specific treatment circumstances

EUROPEAN CENTRE FOR GUIDELINES DEVELOPMENT

European Dermatology Forum

CHARITÉ

d:EBM

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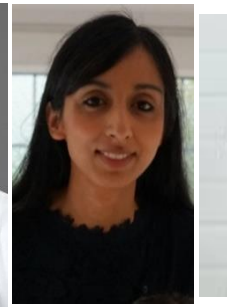
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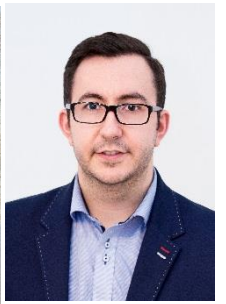
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OVERVIEW OF MAIN RECOMMENDATION

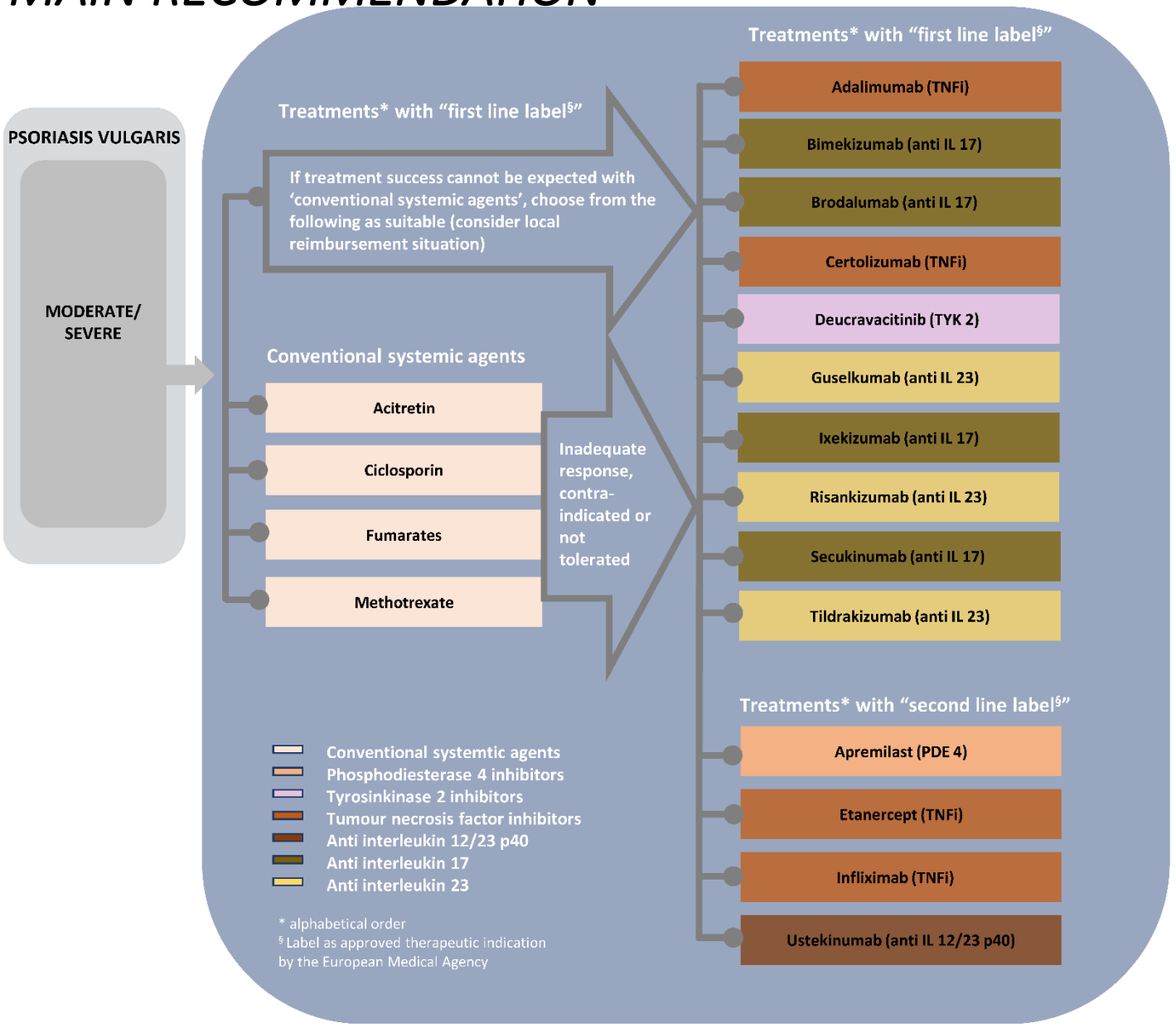

FIGURE 1: OVERVIEW OF TREATMENT OPTIONS FOR PLAQUE TYPE PSORIASIS ARRANGED BY THE LABEL AS APPROVED BY EUROPEAN MEDICAL AGENCY.

WORDING OF RECOMMENDATIONS

Strength	Wording	Symbols	Implications
Strong recommendation **for** the use of an intervention	'We recommend . . .'	↑↑	We believe that all or almost all informed people would make that choice. Clinicians will have to spend less time on the process of decision-making, and may devote that time to overcome barriers to implementation and adherence. In most clinical situations, the recommendation may be adopted as a policy.
Weak recommendation **for** the use of an intervention	'We suggest . . .'	↑	We believe that most informed people would make that choice, but a substantial number would not. Clinicians and health care providers will need to devote more time on the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making requires substantial debate.
No recommendation with respect to an intervention	'We cannot make a recommendation with respect to . . .'	0	At the moment, a recommendation in favour or against an intervention cannot be made due to certain reasons (e.g. no reliable evidence data available, conflicting outcomes, etc.)
Weak recommendation **against** the use of an intervention	'We suggest against . . .'	↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
Strong recommendation **against** the use of an intervention	'We recommend against . . .'	↓↓	We believe that all or almost all informed people would make a choice against that intervention. This recommendation can be adopted as a policy in most clinical situations.

INITIATION AND SELECTION OF A SYSTEMIC TREATMENT

We **recommend** to take efficacy and safety (see **Figure 1** /Cochrane Review [33] and drug chapters), time until onset of treatment response, comorbidities (see decision grids, section Guidance for specific clinical and comorbid situations), and individual patient factors into account when choosing a systemic treatment for moderate or severe psoriasis. In addition, national regulations and reimbursement circumstances need to be taken into consideration and treatment algorithms should be developed on a national level.	↑↑	STRONG CONSENSUS[1] 100 % Agreement EVIDENCE AND CONSENSUS BASED (SEE METHODS AND EVIDENCE SECTION)
We **recommend** the initiation of systemic treatment in patients with moderate to severe (as defined in each country, see also section "Defining disease severity") psoriasis.* **UV therapy is not part of this guideline but it is recommended as an alternative induction therapy if suitable.*	↑↑	

100 % Agreement

...IATION AND SELECTION OF A SYSTEMIC TREATMENT

For most patients who require systemic treatment, we **recommend** choosing a treatment from the group of the 'conventional systemic agents'.	↑↑	CONSENSUS[1] 91%  EVIDENCE AND CONSENSUS BASED (SEE METHODS AND EVIDENCE SECTION)

For cases of severe disease, we **suggest** following **Figure 1**.	↑	STRONG CONSENSUS[1] 100 % Agreement EVIDENCE AND CONSENSUS BASED (SEE METHODS AND EVIDENCE SECTION)
In cases of inadequate response, contra-indication or intolerability we **recommend** following **Figure 1**.	↑↑	

League table below: Short term (8-24 weeks), RR and 95% CI; RRs larger than 1 for the lower triangle and smaller than 1 for the upper triangle favour the treatment on the left. Certainty of evidence high (highlighted in green), moderate (in blue), low (in yellow) and very low (in red). Source: Sbidian et al. 2022

Cochrane Review 'Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis (Review) ' by Emilie Sbidian and colleagues, May 2022, Figure 76

Justification

All treatment options were found to be efficacious when compared to placebo.

Recommendations were drafted along the line of drug licensing, taking practical aspect of reimbursement into account.

National societies may develop different recommendations reflecting the national reimbursement situation.

Following the label, for most patients a 'conventional' is considered as the first treatment option. Taking into consideration the higher efficacy of approved European Medical Agency (EMA) first label biologics, a "first line use" of biologics is considered in patients with severe psoriasis. For the selection of a treatment among the 'conventionals', first line biologics and biologics / small molecules in general, many different factors need to be taken into account (see also "specific treatment circumstances") and no clear hierarchy has been decided upon by the guideline group.

Serious adverse events

Number of participants (studies)	1693 (6)	1730 (4)	5775 (7)	2930 (8)	8459 (20)	313 (1)	4579 (5)	4467 (7)	11342 (16)	2217 (3)	267 (1)	5440 (11)	1323 (5)	8464 (14)	127 (1)	120 (1)	2676 (7)	213 (1)	1130 (2)	-	
1693 (6)	IFX	2.26 (0.81,6.33)	1.30 (0.57,2.97)	1.62 (0.69,3.76)	1.11 (0.50,2.45)	0.95 (0.16,5.50)	1.14 (0.47,2.78)	1.31 (0.58,2.95)	1.22 (0.55,2.71)	1.49 (0.52,4.28)	1.94 (0.18,20.45)	1.17 (0.51,2.67)	1.69 (0.57,5.01)	1.48 (0.66,3.33)	0.21 (0.01,4.01)	**14.82 (1.5,143.4)**	1.38 (0.56,3.44)	1.49 (0.06,38.93)	1.35 (0.45,4.07)	1.18 (0.57,2.43)	19 per 1000
2473 (5)	1.66 (0.68,4.03)	BIME	0.58 (0.25,1.31)	0.72 (0.31,1.63)	0.49 (0.23,1.07)	0.42 (0.07,2.44)	0.51 (0.21,1.22)	0.58 (0.26,1.29)	0.54 (0.25,1.15)	0.66 (0.23,1.91)	0.86 (0.08,9.07)	0.52 (0.24,1.11)	0.75 (0.25,2.23)	0.66 (0.29,1.49)	0.09 (0.00,1.78)	6.56 (0.68,63.61)	0.61 (0.24,1.53)	0.66 (0.03,17.25)	0.60 (0.20,1.81)	0.52 (0.25,1.09)	3 per 1000
5775 (7)	1.66 (0.68,4.03)	1.00 (0.91,1.11)	IXE	1.24 (0.70,2.20)	0.85 (0.53,1.36)	0.73 (0.14,3.79)	0.88 (0.46,1.68)	1.00 (0.64,1.58)	0.94 (0.58,1.53)	1.14 (0.49,2.67)	1.49 (0.15,14.54)	0.90 (0.53,1.54)	1.30 (0.52,3.21)	1.14 (0.71,1.82)	0.16 (0.01,2.90)	**11.39 (1.3,101.6)**	1.06 (0.54,2.10)	1.14 (0.05,28.29)	1.04 (0.41,2.62)	0.91 (0.61,1.36)	16 per 1000
2930 (8)	1.75 (0.72,4.24)	1.05 (0.95,1.17)	1.05 (0.94,1.18)	RISAN	0.69 (0.42,1.11)	0.59 (0.11,3.07)	0.71 (0.37,1.37)	0.81 (0.47,1.38)	0.76 (0.48,1.20)	0.92 (0.38,2.24)	1.20 (0.12,11.78)	0.72 (0.43,1.21)	1.04 (0.41,2.63)	0.92 (0.52,1.62)	0.13 (0.01,2.34)	**9.17 (1.02,82.36)**	0.86 (0.42,1.73)	0.92 (0.04,22.88)	0.84 (0.33,2.14)	0.73 (0.47,1.13)	10 per 1000
9202 (21)	1.91 (0.79,4.63)	**1.15 (1.08,1.23)**	**1.15 (1.06,1.25)**	**1.09 (1.00,1.20)**	SECU	0.86 (0.17,4.31)	1.03 (0.57,1.86)	1.18 (0.82,1.69)	1.10 (0.75,1.61)	1.34 (0.58,3.09)	1.75 (0.18,16.83)	1.06 (0.66,1.69)	1.52 (0.63,3.65)	1.34 (0.83,2.15)	0.19 (0.01,3.36)	**13.35 (1.5,117.6)**	1.25 (0.66,2.36)	1.34 (0.05,32.88)	1.22 (0.50,2.98)	1.06 (0.77,1.47)	19 per 1000
313 (1)	1.96 (0.79,4.89)	1.18 (0.93,1.50)	1.18 (0.93,1.50)	1.12 (0.88,1.43)	1.03 (0.82,1.29)	SONELO	1.20 (0.22,6.46)	1.37 (0.27,7.06)	1.29 (0.25,6.56)	1.56 (0.26,9.27)	2.04 (0.13,32.09)	1.23 (0.24,6.40)	1.78 (0.30,10.71)	1.56 (0.30,8.09)	0.22 (0.01,5.85)	**15.61 (1.1,227.9)**	1.46 (0.27,7.93)	1.57 (0.04,55.24)	1.42 (0.23,8.64)	1.24 (0.25,6.16)	26 per 1000
4579 (5)	2.08 (0.86,5.07)	**1.26 (1.12,1.41)**	**1.25 (1.11,1.42)**	**1.19 (1.05,1.36)**	1.09 (0.98,1.21)	1.06 (0.83,1.36)	BRODA	1.14 (0.61,2.14)	1.07 (0.61,1.87)	1.30 (0.51,3.30)	1.70 (0.17,16.90)	1.02 (0.54,1.95)	1.48 (0.56,3.87)	1.30 (0.68,2.46)	0.18 (0.01,3.35)	**12.95 (1.4,118.3)**	1.21 (0.57,2.58)	1.30 (0.05,32.69)	1.18 (0.44,3.14)	1.03 (0.62,1.73)	18 per 1000
4467 (7)	2.08 (0.86,5.05)	**1.26 (1.16,1.36)**	**1.25 (1.16,1.35)**	**1.19 (1.08,1.32)**	**1.09 (1.02,1.16)**	1.06 (0.84,1.34)	1.00 (0.89,1.12)	GUSEL	0.94 (0.59,1.48)	1.14 (0.48,2.68)	1.49 (0.15,14.44)	0.90 (0.56,1.44)	1.29 (0.53,3.18)	1.14 (0.68,1.89)	0.16 (0.01,2.88)	**11.36 (1.3,101.0)**	1.06 (0.54,2.07)	1.14 (0.05,28.14)	1.03 (0.41,2.59)	0.90 (0.62,1.33)	17 per 1000
11063 (16)	**2.66 (1.09,6.44)**	**1.60 (1.48,1.73)**	**1.60 (1.46,1.74)**	**1.52 (1.38,1.67)**	**1.39 (1.31,1.47)**	**1.35 (1.07,1.71)**	**1.28 (1.17,1.39)**	**1.28 (1.18,1.38)**	USK	1.22 (0.53,2.82)	1.59 (0.16,15.33)	0.96 (0.59,1.56)	1.38 (0.57,3.33)	1.21 (0.75,1.96)	0.17 (0.01,3.06)	**12.14 (1.4,107.1)**	1.13 (0.59,2.16)	1.22 (0.05,29.92)	1.11 (0.45,2.72)	0.97 (0.69,1.36)	15 per 1000
2217 (3)	**2.70 (1.09,6.73)**	**1.63 (1.26,2.10)**	**1.63 (1.27,2.08)**	**1.55 (1.19,2.01)**	**1.41 (1.10,1.81)**	1.38 (0.98,1.93)	**1.30 (1.00,1.69)**	**1.30 (1.01,1.67)**	1.02 (0.79,1.31)	TILDRA	1.31 (0.12,14.02)	0.79 (0.33,1.89)	1.14 (0.37,3.50)	1.00 (0.46,2.18)	0.14 (0.01,2.74)	**9.98 (1.01,98.41)**	0.93 (0.36,2.41)	1.00 (0.04,26.56)	0.91 (0.29,2.85)	0.80 (0.36,1.74)	14 per 1000
267 (1)	3.59 (0.42,30.37)	2.16 (0.31,15.30)	2.16 (0.31,15.26)	2.06 (0.29,14.54)	1.88 (0.27,13.26)	1.83 (0.26,13.10)	1.72 (0.24,12.19)	1.72 (0.24,12.18)	1.35 (0.19,9.55)	1.33 (0.19,9.50)	DEUCRAVA	0.60 (0.06,5.87)	0.87 (0.08,9.43)	0.76 (0.08,7.42)	0.11 (0.00,4.08)	7.63 (0.3,170.4)	0.71 (0.07,7.17)	0.77 (0.02,37.57)	0.70 (0.06,7.59)	0.61 (0.06,5.71)	10 per 1000
5376 (10)	**2.89 (1.19,7.03)**	**1.75 (1.59,1.91)**	**1.74 (1.57,1.93)**	**1.66 (1.50,1.83)**	**1.51 (1.39,1.65)**	**1.48 (1.16,1.88)**	**1.39 (1.22,1.58)**	**1.39 (1.29,1.50)**	1.09 (0.99,1.20)	1.07 (0.83,1.38)	0.81 (0.11,5.70)	ADA	1.44 (0.58,3.56)	1.26 (0.73,2.18)	0.18 (0.01,3.21)	**12.65 (1.4,112.7)**	1.18 (0.60,2.33)	1.27 (0.05,31.39)	1.15 (0.46,2.90)	1.01 (0.68,1.50)	17 per 1000
1323 (5)	**3.77 (1.50,9.53)**	**2.28 (1.69,3.07)**	**2.27 (1.69,3.05)**	**2.16 (1.59,2.93)**	**1.98 (1.47,2.65)**	**1.93 (1.33,2.79)**	**1.81 (1.33,2.47)**	**1.81 (1.35,2.44)**	**1.42 (1.06,1.91)**	1.40 (0.98,1.99)	1.05 (0.15,7.57)	1.30 (0.96,1.77)	CERTO	0.88 (0.36,2.14)	0.12 (0.01,2.43)	8.78 (0.88,87.57)	0.82 (0.31,2.19)	0.88 (0.03,23.55)	0.80 (0.25,2.56)	0.70 (0.31,1.58)	13 per 1000
9759 (16)	**4.71 (1.94,11.44)**	**2.84 (2.50,3.22)**	**2.83 (2.54,3.16)**	**2.70 (2.35,3.10)**	**2.47 (2.20,2.76)**	**2.40 (1.87,3.10)**	**2.26 (1.96,2.61)**	**2.26 (2.01,2.54)**	**1.77 (1.58,1.99)**	**1.74 (1.39,2.18)**	1.31 (0.19,9.29)	**1.63 (1.43,1.86)**	1.25 (0.95,1.65)	ETA	0.14 (0.01,2.54)	**10.00 (1.12,89.10)**	0.93 (0.49,1.80)	1.00 (0.04,24.82)	0.91 (0.36,2.29)	0.80 (0.54,1.18)	15 per 1000
172 (2)	**7.13 (1.08,47.09)**	4.30 (0.80,23.11)	4.29 (0.80,23.05)	4.08 (0.76,21.96)	3.73 (0.69,20.03)	3.64 (0.67,19.82)	3.42 (0.64,18.42)	3.42 (0.64,18.39)	2.68 (0.50,14.42)	2.64 (0.48,14.37)	1.99 (0.15,25.89)	2.46 (0.46,13.24)	1.89 (0.34,10.37)	1.51 (0.28,8.14)	CICLO	**71.47 (2.0,2585.3)**	6.68 (0.4,124.4)	7.17 (0.1,522.0)	6.51 (0.3,129.5)	5.69 (0.3,100.6)	25 per 1000
388 (5)	**7.20 (1.17,44.37)**	4.34 (0.87,21.58)	4.33 (0.87,21.53)	4.12 (0.83,20.51)	3.77 (0.76,18.71)	3.67 (0.73,18.53)	3.46 (0.69,17.21)	3.46 (0.70,17.18)	2.71 (0.55,13.47)	2.66 (0.53,13.43)	2.01 (0.16,24.86)	2.49 (0.50,12.37)	1.91 (0.38,9.70)	1.53 (0.31,7.60)	1.01 (0.61,1.68)	MTX	0.09 (0.01,0.86)	0.10 (0.00,4.68)	0.09 (0.01,0.91)	0.08 (0.01,0.68)	7 per 1000
2113 (5)	**6.53 (2.34,18.19)**	**3.94 (2.29,6.77)**	**3.93 (2.29,6.74)**	**3.74 (2.17,6.45)**	**3.42 (1.99,5.86)**	**3.33 (1.86,5.98)**	**3.14 (1.82,5.41)**	**3.14 (1.83,5.38)**	**2.46 (1.43,4.22)**	**2.42 (1.35,4.31)**	1.82 (0.24,13.73)	**2.26 (1.31,3.88)**	1.73 (0.95,3.15)	1.39 (0.81,2.37)	0.92 (0.16,5.31)	0.91 (0.17,4.88)	APRE	1.07 (0.04,27.19)	0.98 (0.36,2.65)	0.85 (0.49,1.48)	15 per 1000
333 (2)	**11.18 (3.47,35.99)**	**6.74 (3.04,14.92)**	**6.72 (3.04,14.89)**	**6.40 (2.89,14.19)**	**5.85 (2.65,12.93)**	**5.70 (2.50,13.00)**	**5.37 (2.42,11.91)**	**5.37 (2.43,11.87)**	**4.21 (1.90,9.31)**	**4.13 (1.81,9.43)**	3.11 (0.38,25.35)	**3.86 (1.74,8.55)**	**2.96 (1.28,6.85)**	**2.37 (1.07,5.26)**	1.57 (0.25,9.91)	1.55 (0.26,9.14)	1.71 (0.67,4.40)	NETA	0.91 (0.03,24.40)	0.79 (0.03,19.17)	26 per 1000
764 (2)	**11.52 (3.58,37.11)**	**6.95 (3.14,15.39)**	**6.93 (3.13,15.35)**	**6.60 (2.98,14.63)**	**6.03 (2.73,13.33)**	**5.88 (2.58,13.40)**	**5.53 (2.49,12.28)**	**5.53 (2.50,12.24)**	**4.34 (1.96,9.59)**	**4.26 (1.87,9.72)**	3.21 (0.39,26.13)	**3.98 (1.80,8.82)**	**3.05 (1.32,7.07)**	**2.45 (1.10,5.42)**	1.62 (0.30,8.80)	1.60 (0.32,8.06)	1.76 (0.69,4.54)	1.03 (0.34,3.09)	FUM	0.87 (0.38,2.01)	17 per 1000
-	**50.19 (20.9,120.5)**	**30.27 (25.5,36.0)**	**30.19 (25.4,35.9)**	**28.75 (24.0,34.4)**	**26.26 (22.3,31.0)**	**25.60 (19.4,33.9)**	**24.10 (20.1,29.0)**	**24.11 (20.4,28.5)**	**18.90 (16.0,22.3)**	**18.57 (14.0,24.6)**	**13.99 (1.99,98.10)**	**17.35 (14.6,20.6)**	**13.30 (9.65,18.32)**	**10.65 (8.89,12.77)**	**7.04 (1.32,37.50)**	**6.97 (1.42,34.34)**	**7.69 (4.48,13.18)**	**4.49 (2.07,9.76)**	**4.36 (2.01,9.46)**	PBO	26 per 1000
	443 per 1000	880 per 1000	422 per 1000	415 per 1000	360 per 1000	210 per 1000	329 per 1000	388 per 1000	258 per 1000	256 per 1000	210 per 1000	267 per 1000	182 per 1000	146 per 1000	148 per 1000	147 per 1000	110 per 1000	123 per 1000	55 per 1000	25 per 1000	Anticipated absolute effects

PASI 90

OVERVIEW OF TREATMENT OPTIONS AND THE EXPERT ASSESSMENT OF THEIR SUITABILITY IN SPECIFIC TREATMENT CIRCUMSTANCES

Symbols	Implications
↑↑	We believe that all or almost all informed people would make that choice.
↑	We believe that most informed people would make that choice, but a substantial number would not.
	See background text and specific recommendations
↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
↓↓	We believe that all or almost all informed people would make a choice against that choice.

OVERVIEW OF TREATMENT OPTIONS AND THE EXPERT ASSESSMENT OF THEIR SUITABILITY IN SPECIFIC TREATMENT CIRCUMSTANCES

Therapy / Specific circumstances	Conventional systemic agents						tnf inhibitors				anti-IL12/23	anti-IL17				anti-IL23		
	Acitretin	Ciclosporin	Fumarates	Methotrexate	Apremilast	Deucravacitin	Etanercept	Infliximab	Adalimumab	Certolizumab	Ustekinumab	Secukinumab	Ixekizumab	Brodalumab	Bimekizumab	Guselkumab	Tildrakizumab	Risankizumab
Concomitant psoriatic arthritis				↑ first line peripheral active joint involvement	↑		↑↑								has been approved for PsA 06/23, evaluation pending	↑↑		↑↑
Chronic inflammatory bowel disease: Crohn's Disease	↑ especially cases with mild paradoxical psoriasis			↑ 2nd choice oral treatment			↑↑ 1st choice					↓				↑ 2nd choice if anti-TNF alpha not suitable		
Chronic inflammatory bowel disease: Ulcerative colitis	↑ especially cases with mild paradoxical psoriasis	↑ 2nd choice oral treatment			↑ 2nd choice oral treatment		↑↑ 1st choice				↑↑ 1st choice	↓				↑ 2nd choice if anti-TNF alpha not suitable		
Diabetes mel./ metabolic syndrome		consider alternatives		consider alternatives														
Dyslipidaemia	↓																	
Advanced heart failure	↑	↓		↑	↑		↓↓					↑				↑		
Heart Disease: Ischemic heart disease	↓			↑			↑											
Concomitant latent / treated TB	↑		↑		↑		↓↓					↑				↑		
Pregnancy	↓↓	↑ preferred conventional	↓	↓↓	↓	↓				↑ preferred choice biologic								

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CHARITÉ d:EBM
Oct 2023

How should psoriasis patients with concomitant psoriatic arthritis be managed?

We **recommend** interdisciplinary cooperation with a rheumatologist for the confirmation of the diagnosis of psoriatic arthritis and the selection of a suitable treatment whenever needed.	↑↑	STRONG CONSENSUS[1]  EXPERT CONSENSUS

Treatment initiation

We **recommend** starting treatment early to prevent progression of disease and erosive destruction of joints.	↑↑	STRONG CONSENSUS  EXPERT CONSENSUS

How should psoriasis patients with concomitant psoriatic arthritis be managed?

Conventional synthetic DMARDs (e.g., MTX)

We **suggest** monotherapy with a synthetic DMARD (e.g. MTX) as first-line treatment for most patients with moderate to severe psoriasis of the skin and active joint involvement (PsA).	↑	STRONG CONSENSUS 100 % Agreement EVIDENCE AND EXPERT CONSENSUS TABLE **1**

Biological DMARDs

For patients with an inadequate response after at least one synthetic DMARD, we **recommend** using a biological DMARD as monotherapy or in combination with a synthetic DMARD. In cases of severe active joint involvement (PsA) where a sufficient response cannot be expected with the use of a conventional treatment, we recommend using a biologic as first-line therapy.	↑↑	STRONG CONSENSUS 100 % Agreement EVIDENCE AND EXPERT CONSENSUS TABLE **1**
When choosing a bDMARD for patients with moderate to severe psoriasis of the skin and active joint involvement (PsA), we **recommend** taking into account aspects of efficacy with regard to skin and the joints, comorbidity, practicability and safety.	↑↑	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS

How should psoriasis patients with concomitant psoriatic arthritis be managed?

Small molecules

We **suggest** using apremilast for patients with moderate to severe psoriasis of the skin and active joint involvement (PsA) if an oral treatment is desired or if other systemic agents have led to an inadequate response or if they are contraindicated or not tolerated.	↑	STRONG CONSENSUS  EVIDENCE AND EXPERT CONSENSUS

Axial spondyloarthritis

We **suggest** using TNFi or IL-17 antagonists for patients with moderate to severe psoriasis of the skin and concomitant PsA manifestation in the form of axial involvement or enthesitis.	↑	STRONG CONSENSUS  EXPERT CONSENSUS

	Patients achieving ARC20 after 12-24 weeks			Patients with at least one adverse event		
	RR	95% CI	Certainty Evidence (GRADE)	RR	95% CI	Certainty Evidence (GRADE)
Head-to-head comparisons:						
ADA 40 mg Q2W+ MTX 15 mg p.o./s.c. QW vs. MTX up to 20-25 mg p.o./s.c. or highest tolerable dose QW	2.06	1.55 to 2.73	LOW	1.08	0.88 to 1.32	VERY LOW
ADA 40mg EOW (1) vs. SEC 300mg LD then Q4W	0.92	0.82 to 1.02	MODERATE	1.02	0.95 to 1.10	MODERATE
APR vs. MTX (no dosage given)	0.83	0.42 to 1.66	VERY LOW	0.53	0.16 to 1.76	VERY LOW
ETA 50mg QW + MTX up to 20mg QW vs. MTX up to 20mg QW	1.28	1.11 to 1.48	LOW	1.01	0.92 to 1.11	MODERATE
INF 5mg/kg w0, 2, 6, 14 + MTX 15mg QW vs. MTX 15mg/ QW	1.40	1.07 to 1.84	VERY LOW	1.65	1.08 to 2.52	VERY LOW
IXE 80mg Q2W (LD 160mg w0) vs. ADA 40mg EOW (1)	1.08	0.86 to 1.36	LOW	1.02*	0.83 to 1.25	MODERATE
Placebo comparisons:						
ADA 40mg EOW (2)	2.08	1.52 to 2.86	MODERATE	1.07	0.83 to 1.39	MODERATE
APR 30mg BID	2.01	1.69 to 2.40	MODERATE	1.24	1.12 to 1.36	LOW
CZP 400mg LD then 200mg Q2W	2.71	1.95 to 3.76	MODERATE	1.01*	0.86 to 1.19	MODERATE
CZP 400mg LD then 400mg Q4W (3)	2.36	1.68 to 3.31	MODERATE	1.05*	0.90 to 1.23	MODERATE
ETA 25mg BIW	5.47	3.27 to 9.16	LOW	no data		
GUS 100mg LD then Q8W (4)	2.13	1.82 to 2.50	HIGH	0.99	0.87 to 1.13	HIGH
INF 5mg/kg w0, 2, 6, 14	4.38	2.24 to 8.56	MODERATE	1.13	0.87 to 1.47	LOW
IXE 80mg Q2W (LD160mg w0)	2.21	1.71 to 2.86	MODERATE	1.39*	1.09 to 1.78	LOW
MTX 7.5mg to 10mg to 15mg	1.82	0.97 to 3.40	LOW	no data		
RZB 150mg w0, 4, 16	1.76	1.56 to 2.00	HIGH	1.03*	0.92 to 1.15	HIGH
SEC 300mg + LD vs. PBO (ACR20 w16-24)	2.55	2.09 to 3.10	MODERATE	1.01	0.91 to 1.11	MODERATE
SEC 300mg + LD vs. PBO (ACR20 w12)	2.74	1.93 to 3.89	MODERATE	0.83	0.65 to 1.06	LOW
UST 45mg	1.95	1.52 to 2.50	HIGH	no data		
UST 90mg (5)	2.26	1.80 to 2.82	MODERATE	0.96	0.75 to 1.24	VERY LOW

1 - 80mg LD only for pts. with moderate-to-severe PsO
2 - No LD of 80mg (this would be the case for PsO)
3 - For psoriasis vulgaris, 400mg Q2W can also be considered
4 - For patients at high risk of joint damage according to clinical judgement, a dose of 100 mg every 4 weeks may be considered (SMPc)
5- For Pso patient with >=100kg (dosis not licensed for PsA); one study reported induction dose of QW (weeks 0-3).
*treatment emergent adverse events

How should psoriasis patients be managed with concomitant inflammatory bowel disease (last update: 10/2021)?

We recommend working in collaboration with the treating gastroenterologist when prescribing a systemic therapy in psoriasis patients with concomitant chronic inflammatory bowel disease.	↑↑	STRONG CONSENSUS EXPERT CONSENSUS 100 % Agreement
In patients with psoriasis and active IBD or a history of IBD, we **recommend** to preferentially use approved targeted therapies with a documented efficacy in these conditions: *Crohn's disease:* anti-TNF (infliximab, adalimumab, certolizumab) and anti-IL-12/23p40 (ustekinumab). *Ulcerative colitis:* anti-TNF (infliximab, adalimumab) and anti-IL-12/23p40 (ustekinumab).	↑↑	
If these first-choice treatments cannot be used, **we suggest** the following treatments to be considered as second choice targeted treatment options in patients with psoriasis and IBD: *Crohn's disease:* Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab) *Ulcerative colitis:* Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab)	↑	
If these first-choice treatments cannot be used, we **suggest** the following treatments to be considered as second choice oral treatment options in patients with psoriasis and IBD *Crohn's disease:* Methotrexate *Active ulcerative colitis:* Ciclosporine (preferred), apremilast (also possible)	↑	
In combination with other treatments, we **suggest** acitretin as an adjunct therapy for patients with IBD and psoriasis, especially in cases with mild paradoxical psoriasis	↑	
We suggest against the use of anti IL 17 antibodies in patients with inflammatory bowel disease.	↓	

How should psoriasis patients be managed with concomitant inflammatory bowel disease (last update: 10/2021)?

Therapy / Specific circumstances	Conventional systemic agents			
	Acitretin	Ciclosporin	Fumarates	Methotrexate
Chronic inflammatory bowel disease: Crohn's Disease	↑ especially cases with mild paradoxical psoriasis			↑ 2nd choice oral treatment
Chronic inflammatory bowel disease: Ulcerative colitis	↑ especially cases with mild paradoxical psoriasis	↑ 2nd choice oral treatment		

Therapy / Specific circumstances			tnf inhibitors				anti-IL12/23	anti-IL17				anti-IL23		
	Apremilast	Deucravacitinib	Etanercept	Infliximab	Adalimumab	Certolizumab	Ustekinumab	Secukinumab	Ixekizumab	Brodalumab	Bimekizumab	Guselkumab	Tildrakizumab	Risankizumab
Chronic inflammatory bowel disease: Crohn's Disease			↑↑ 1st choice					↓				↑ 2nd choice if anti-TNF alpha not suitable		
Chronic inflammatory bowel disease: Ulcerative colitis	↑ 2nd choice oral treatment		↑↑ 1st choice				↑↑ 1st choice	↓				↑ 2nd choice if anti-TNF alpha not suitable		

EUROPEAN CENTRE FOR GUIDELINES DEVELOPMENT
European Dermatology Forum
Charité d:EBM
Oct 2023

How should psoriasis patients with a history of malignancies be managed?

We **recommend** taking the burden of psoriasis, and the risk of cancer worsening or recurrence (pre-cancer vs low risk vs high risk) into account for shared therapeutic decision making.	↑↑	STRONG CONSENSUS[1] 
For patients with recent malignancy we **recommend** topical therapies, phototherapy (narrow band UVB) * and/or acitretin. *except patients with a recent, and/or high risk of cutaneous malignancy	↑↑	EXPERT CONSENSUS

How should psoriasis patients with a history of malignancies be managed?

We **recommend** to discuss the decision to initiate immunosuppressive therapies, in psoriasis patients with a current or recent diagnosis of cancer in the previous five years case-by-case with cancer specialists and to reach an informed decision, respecting the patient's preference.	↑↑	STRONG CONSENSUS[1]  EXPERT CONSENSUS
In case of inadequate response to topical therapies, phototherapy, (narrow band UVB) and/or acitretin we **suggest** using MTX in psoriasis patients with a previous history of cancer.* *(*for patients with history of non melanoma skin cancer, see background text)*	↑	

How should psoriasis patients with a history of malignancies be managed?

We **suggest** apremilast can be used in psoriasis patients with a previous history of cancer despite the lack of long term experience based on pathophysiological considerations on a case-by-case basis including discussion with cancer specialist	↑	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS
We **suggested against** using ciclosporin in psoriasis patients with a previous history of cancer.	↓	
We **suggest** TNFi, ustekinumab can be used based on existing safety data on a case-by-case basis including discussion with cancer specialist. We **suggest** anti-IL17, anti-IL23 can be used in psoriasis patients with a previous history of cancer despite the lack of long term experience based on pathophysiological considerations on a case-by-case basis including discussion with a cancer specialist.	↑	

How should psoriasis patients with a history of depression and/or suicidal ideation be managed?

We **recommend** to be aware of signs and symptoms of anxiety and depression in patients with psoriasis and monitor for symptoms of depression and/or suicidal ideation or anxiety during systemic treatments for psoriasis especially in those with a history of any of the above.	↑↑	STRONG CONSENSUS[1] 100 % Agreement
We **suggest** using alternatives to brodalumab and apremilast in patients with a history of depression and/or suicidal ideation.	↑	EXPERT CONSENSUS

How should psoriasis patients with diabetes mellitus be managed?

We **suggest** considering alternatives to methotrexate in people with type 2 diabetes (if accompanied by metabolic syndrome and/or evidence of liver damage) when alternative treatments can be prescribed.	↑	STRONG CONSENSUS[1]  EXPERT CONSENSUS
We **suggest** considering alternatives to ciclosporine in people with type 2 diabetes (if accompanied by metabolic syndrome and/or evidence of liver damage) when alternative treatments can be prescribed.	↑	STRONG CONSENSUS[1]  EXPERT CONSENSUS
We **suggest against** using acitretin as a first line treatment in patients with dyslipidaemia.	↓	STRONG CONSENSUS[2]  EXPERT CONSENSUS

HEART DISEASE: HOW SHOULD PSORIASIS PATIENTS WITH ISCHAEMIC HEART DISEASE AND/OR CONGESTIVE HEART FAILURE BE MANAGED?

We **suggest against** cyclosporine or acitretin as preferred treatments in patients with psoriasis and ischemic heart disease.	↓	STRONG CONSENSUS[1] 100 % Agreement
We **suggest** methotrexate as preferred first-line therapy in patients with psoriasis and ischemic heart disease* if other patient characteristics do not preclude its use.	↑	EXPERT CONSENSUS
We **suggest** TNFi, ustekinumab, and IL-17 inhibitors as preferred targeted therapies in patients with psoriasis and ischemic heart disease*.	↑	

HEART DISEASE: HOW SHOULD PSORIASIS PATIENTS WITH ISCHAEMIC HEART DISEASE AND/OR CONGESTIVE HEART FAILURE BE MANAGED?

We **suggest against** using cyclosporine in patients with psoriasis and advanced congestive heart failure.	↓	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS
We **suggest** that methotrexate, acitretin and apremilast are considered as treatment in patients with psoriasis and advanced congestive heart failure*.	↑	
We **suggest** that ustekinumab, inhibitors of IL-17 and of IL-23 are considered as treatment in patients with psoriasis and advanced congestive heart failure*.	↑	
We **recommend against** using TNFi in patients with psoriasis and advanced congestive heart failure	↓↓	
We **recommend** discussing the choice of a systemic therapy in psoriasis patients with **advanced** congestive heart failure with a cardiologist.	↑↑	

Heart failure (HF) is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress.

How should psoriasis patients with kidney failure / renal impairment be managed?

We **recommend** ensuring an accurate assessment of renal function in any psoriasis patient with known or suspected chronic kidney disease prior to therapy.	↑↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS
We **recommend** working in collaboration with the nephrologist when prescribing systemic therapy in any psoriasis patient with chronic kidney disease of stage 3 (eGFR <60 mL/min/1.73 m^2) or more.	↑↑	
We **suggest** acitretin*, apremilast, fumarates*, methotrexate* **may be used** in psoriasis patients with **mild to moderate renal impairment** (eGFR ≥30 mL/min/1.73m^2). *(carefull dosing/dose adjustment may be needed)	↑	
We **suggest** using biologics in psoriasis patients with chronic kidney disease and all stages of renal impairment.	↑	
We **recommend against** using ciclosporin, fumarates, or methotrexate in psoriasis patients with **chronic kidney disease and severe renal** impairment (eGFR <30 mL/min/1.73m^2).	↓↓	

WHICH TREATMENTS ARE APPROPRIATE FOR PSORIASIS PATIENTS WITH NEUROLOGICAL DISEASES?

We **suggest** using fumarates in psoriasis patients with multiple sclerosis.	↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS
We **recommend against** using TNFi therapy in psoriasis patients with a diagnosis of multiple sclerosis or other demyelinating disease.	↓↓	
In psoriasis patients with a first-degree relative with multiple sclerosis or other demyelinating disease, we **suggest against** the use of TNFi therapy if other suitable treatment options are available.	↓	

How to screen for tuberculosis before and during biologic treatment?

We **recommend** to do tuberculosis screening according to local regulations.	↑↑	STRONG CONSENSUS[1] 
For pre-screening, we **recommend** anamnesis including tuberculosis history; a chest X-ray; TST and/or IGRA.	↑↑	
We **recommend** remaining alert to the possibility of tuberculosis infection during therapy. This includes taking medical history and might include tuberculosis testing.	↑↑	EXPERT CONSENSUS

HOW TO SCREEN FOR TUBERCULOSIS BEFORE AND DURING BIOLOGIC TREATMENT?

Diagnostic for TB, regardless Bacillus Calmette-Guérin (BCG) vaccination, prior to and during follow up with biologic. One must be alert for TB infections before, during biologic treatment and up to six months after discontinuation. During treatment, rescreening for LTBI is recommended and frequency should be based on patient history and risk of exposure.

1. Patient history:
   - Symptoms suspicious for TB
   - History of TB, adequate treatment
   - Exposure to TB
   - Origin from or recently stayed for a long time in an endemic area
   - High risk patient
   - BCG vaccination

1. Physical examination, to consider:
   - Auscultation of the lungs if symptomatic (not-specific for TB diagnosis)
   - Scar (left) upper arm (may indicate a BCG vaccination)
   - Enlarged lymph nodes, abscess scars

1. Chest X-ray: If a chest X-ray has been conducted **in the past**, the decision to repeat the X-ray should be based on the psoriasis treatment selected, time since the last x-ray, the patient's risk profile, potential exposure or local guidelines.
   - Suspicious for active, LTBI or history of TB?
     → consult pulmonologist if abnormalities

1. TST* and/or IGRA

   - If IGRA and TST are both performed, the IGRA can best be drawn right after the TST is assessed. If drawing is done more than three days after the TST, the TST can booster the IGRA and result in a false-positive response.
   - The recommendation to perform IGRA testing rather than TST testing is strong for those who have received the BCG vaccination.

HOW TO SCREEN FOR TUBERCULOSIS BEFORE AND DURING BIOLOGIC TREATMENT?

Physicians have to be aware that there is still a risk of active tuberculosis under biologic therapy, even if LTBI was correctly treated. Therefore, rescreening on LTBI is preferable during biologic treatment. The frequency should take risk exposure into consideration. Besides medical history, both TST and IGRA are recommended, because of the influence that the biologic may have (false-negative) on these tests. A high index of suspicion should also be maintained for six months following discontinuation.

How to manage psoriasis in patients with positive tuberculosis test results?

We **recommend** discussing the decision to initiate immuno-suppressive therapies in patients with signs of latent tuberculosis with an infectious disease specialist (case-by-case basis).	↑↑	STRONG CONSENSUS[1] 100 % Agreement
As a commonly used procedure in case of latent TB, a treatment with isoniazid can be **recommended** with treatment initiation one month before the start of the immunosuppressive therapy and should be continued for 6 months (for alternatives see Table 48).	↑↑	EXPERT CONSENSUS

Table 48: Therapeutic regimens for LTBI

Drug	Dose	Treatment duration
INH alone (daily)	5 mg/kg; max dose: 300 mg	6-9 months
RIF alone (daily)	10mg/kg; max dose: 600 mg	3-4 months
INH + RIF (daily)	INH: 5 mg/kg; max dose: 300 mg RIF: 10mg/kg; max dose: 600 mg	3-4 months

INH = Isoniazide; RIF Rifampicin, Treatments with pyrazinamide should be avoided (high risk of hepatotoxicity). Based on WHO: Latent tuberculosis infection: updated and consolidated guidelines for programmatic management, 2018.

How to manage psoriasis in patients with positive tuberculosis test results?

Systemic treatments		Screening recommendation as provided in SmPC	Comments
Conventional systemic agents	Acitretin	No	No cases of reactivation have been reported[19]
	Ciclosporin	No	Cases have been reported in organ transplant patients with high doses of CsA [19]
	Fumarates	No	No cases of reactivation have been reported [20,21]
	Methotrexate	Yes	Cases of reactivation have been reported [22]
Phospho-diesterase 4 inhibitor	Apremilast	No	Increased risk has not been reported [23]
Tyrosine-kinase 2 inhibitor	Deucravacitinib	Yes	Uncertain risk of reactivation. No data available yet.
TNFi	Etanercept	Yes	Increased risk of reactivation has been reported [24,25]
	Infliximab	Yes	Increased risk of reactivation has been reported [24,25]
	Adalimumab	Yes	Increased risk of reactivation has been reported [24,25]
	Certolizumab	Yes	Increased risk of reactivation has been reported [19,24]
Anti-IL 12/23	Ustekinumab	Yes	Uncertain risk of reactivation (cases have been reported) [19,26,27]
Anti-IL 17	Secukinumab	Yes	Increased risk has not been reported in clinical trials [26,28]
	Ixekizumab	Yes	Increased risk has not been reported in clinical trials [26]
	Brodalumab	Yes	Increased risk has not been reported in clinical trials [26]
Anti-IL 23	Guselkumab	Yes	Increased risk has not been reported in clinical trials [29]
	Tildrakizumab	Yes	Increased risk has not been reported in clinical trials [30]
	Risankizumab	Yes	Increased risk has not been reported in clinical trials [31]
Reported cases need to be seen in correlation to approval date, especially with years and numbers of psoriasis patients exposed to the drug.			

How to manage psoriasis in patients with positive tuberculosis test results?

We **recommend against** TNFi as a treatment for patients with latent TB unless there are no other suitable treatment options.	↓↓	
We **recommend** remaining alert to signs and symptoms of tuberculosis activation or re-infection during therapy.	↑↑	STRONG CONSENSUS[1] 100 % Agreement
We **suggest** acitretin, apremilast or fumarates or a treatment from the anti-IL-17 and anti-IL-23 group for patients with latent TB that require a systemic antipsoriatic treatment.	↑	EXPERT CONSENSUS

How should psoriasis patients with a wish for pregnancy in the near future or who are pregnant be managed (last update: 10/2021)?

We **suggest** ciclosporin as a first line convention agent in women planning conception and when it is necessary to start systemic therapy during the 2nd and 3rd trimester of pregnancy	↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS
Methotrexate and acitretin are contra-indicated in women planning conception. We **recommend against** using these.	↓↓	
Fumarates and apremilast are contra-indicated in women planning conception. We **suggest against** using these.	↓	
We **recommend** consultation and information sharing across specialties, including with an obstetrician with expertise in caring for pregnant women with medical problems	↑↑	
We **recommend** the collection of maternal exposure to medications and pregnancy outcome data in national safety registries where available.	↑↑	

How should psoriasis patients with a wish for pregnancy in the near future or who are pregnant be managed (last update: 10/2021)?

We **suggest** certolizumab pegol as a first line choice when starting biologic therapy in women planning conception (when a biologic is considered essential to use in pregnancy) and when it is necessary to start a systemic therapy during the second or third trimester.	↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS
We **suggest** stopping biologic therapy in the second and third trimester (except certolizumab pegol) to minimise fetal exposure and limit potential infection risk to the neonate.	↑	
We **suggest against** using live or live attenuated vaccines in infants (up to 6 months of age) whose mothers received biologic therapy beyond 16 weeks gestation, unless the benefit of the vaccination clearly outweighs the theoretical risk of administration.	↓	
We **recommend** consultation and information sharing across specialties, including with an obstetrician with expertise in caring for pregnant women with medical problems	↑↑	
We **recommend** the collection of maternal exposure to medications and pregnancy outcome data in national safety registries where available.	↑↑	

PATERNAL USE (LAST UPDATE: 10/2021)

It is **recommended** that men discontinue methotrexate 3 months before attempting conception. * *EMA recommends 6 months as a means of precaution, the practice of the guideline group differs from this.	↑↑	STRONG CONSENSUS[1]  EXPERT CONSENSUS
As a precaution, it is **suggested** that men taking acitretin use barrier forms of contraception post-conception to limit exposure via direct contact with semen during pregnancy.	↑	
We **recommend** the collection of paternal exposure to medications during conception and pregnancy outcome data in national safety registries where available.	↑↑	

OVERVIEW OF TREATMENT OPTIONS AND THE EXPERT ASSESSMENT OF THEIR SUITABILITY IN SPECIFIC TREATMENT CIRCUMSTANCES

Symbols	Implications
↑↑	We believe that all or almost all informed people would make that choice.
↑	We believe that most informed people would make that choice, but a substantial number would not.
	See background text and specific recommendations
↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
↓↓	We believe that all or almost all informed people would make a choice against that choice.

OVERVIEW OF TREATMENT OPTIONS AND THE EXPERT ASSESSMENT OF THEIR SUITABILITY IN SPECIFIC TREATMENT CIRCUMSTANCES

Therapy / Specific circumstances	Conventional systemic agents						tnf inhibitors				anti-IL12/23	anti-IL17				anti-IL23		
	Acitretin	Ciclosporin	Fumarates	Methotrexate	Apremilast	Deucravacitin	Etanercept	Infliximab	Adalimumab	Certolizumab	Ustekinumab	Secukinumab	Ixekizumab	Brodalumab	Bimekizumab	Guselkumab	Tildrakizumab	Risankizumab
Concomitant psoriatic arthritis				↑ first line peripheral active joint involvement	↑		↑↑								has been approved for PsA 06/23, evaluation pending	↑↑		↑↑
Chronic inflammatory bowel disease: Crohn's Disease	↑ especially cases with mild paradoxical psoriasis			↑ 2nd choice oral treatment				↑↑ 1st choice				↓				↑ 2nd choice if anti-TNF alpha not suitable		
Chronic inflammatory bowel disease: Ulcerative colitis	↑ especially cases with mild paradoxical psoriasis	↑ 2nd choice oral treatment			↑ 2nd choice oral treatment			↑↑ 1st choice			↑↑ 1st choice	↓				↑ 2nd choice if anti-TNF alpha not suitable		
Diabetes mel.I metabolic syndrome		consider alternatives		consider alternatives														
Dyslipidaemia	↓																	
Advanced heart failure	↑	↓		↑	↑		↓↓				↑					↑		
Heart Disease: Ischemic heart disease	↓			↑			↑											
Concomitant latent / treated TB	↑		↑		↑		↓↓					↑				↑		
Pregnancy	↓↓	↑ preferred conventional	↓	↓↓	↓	↓				↑ preferred choice biologic								