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Appendix B: Evidenzreport zur Leitlinie ‚Therapie der Psoriasis vulgaris'

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Die hier enthaltenen Dokumente Appendix 1, 2, 5 und 7 wurden aus dem EUROGUIDERM GUIDELINE ON THE SYSTEMIC TREATMENT OF PSORIASIS VULGARIS– METHODS & EVIDENCE REPORT übernommen. Den vollständige Bericht finden Sie unter https://psoriasis.euroguiderm.eu. Die Verwertungsrechte liegen beim European Dermatology Forum.

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APPENDIX 1 EVIDENCE TO DECISION FRAMEWORK PLAQUE TYPE PSORIASIS

Plaque type psoriasis: Evidence to decision framework

For patients with plaque type psoriasis, what are the clinical effectiveness/efficacy, safety and tolerability of conventionals (acitretin, ciclosporin, fumaric acid esters, methotrexate), biologics (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab or ustekinumab), small molecules (apremilast) compared with each other or with placebo?

POPULATION:

Patients with moderate to severe psoriasis vulgaris

INTERVENTION:

Systemic treatments

Systemic conventional treatments	Small molecules	Tnf inhibitors	Anti-IL12/23	Anti-IL17	Anti-IL23
Acitretin	Apremilast	Adalimumab	Ustekinumab	Brodalumab	Guselkumab
Ciclosporin		Certolizumab		Ixekizumab	Rizankizumab
FAEs		Etanercept		Secukinumab	Tildrakizumab
Methotrexate		Infliximab			

COMPARISON:

All systemic treatments and placebo

MAIN OUTCOMES:

- Psoriasis Area and Severity Index (PASI) 90% improvement
- Proportion of patients that experienced a severe adverse event (SAE)

SETTING:

- Region: Europe (study inclusion not limited to studies done in Europe)
- Setting: clinical and practice (private and public) dermatologists

PERSPECTIVE:

- Population perspective

BACKGROUND:

- Several new treatments have been developed and approved
- New statistical methods have become available to allow for comparisons where no head-to-head RCTs exists
- Knowledge on monitoring and management of new treatment options is limited and physicians need guidance on how to use these
- Many psoriasis patients have significant comorbidity and specific advise is necessary to treat these patients
- Hence, the objectives of the guideline are to:
  - Include new treatments and the evidence that has become available
  - Update the recommendations regarding biologic systemic treatment options (Part 1)
  - Develop a treatment algorithms including biologic and nonbiologic systemic treatment options
  - Provide clear recommendations on how to best monitor and manage patients considering the available treatment options
  - Develop several, short guidance documents with visual tools for ease of implementation
  - Provide guidance on the treatment of special populations and difficult clinical situations (mostly expert consensus; Part 2)

Evidence synthesis in cooperation with:
Sbidian_E, Chaimani_A, Afach_S, Doney_L, Dressler_C, Hua_C, Mazaud_C, Phan_C, Hughes_C, Riddle_D, Naldi_L, Garcia-Doval_I, LeCleach_L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD011535. DOI: 10.1002/14651858.CD011535.pub3.(1)

CONFLICT OF INTERESTS:	Less than 50% of the guideline development committee declared to have personal-financial conflicts of interests (see Methods & Evidence report of this guideline). For the Cochrane Review author groups' declaration of interests, see page 594 of the review.

Needs Assessment

RESEARCH EVIDENCE

- Differences between psoriasis guidelines exists, such as in the evaluation of the evidence (2)
- "There exists a disconnect between the European psoriasis treatment guidelines and the various central and eastern European country-specific biologic coverage eligibilities" (3);
- „Our results [comparing Czech Psoriasis register with others e.g. PsoBest] found a similar or higher prevalence of comorbidities, long disease duration, and high impact on the quality of life among patients included in Western European registries."(4);

Desirable Effects

How substantial are the desirable anticipated effects?

RESEARCH EVIDENCE

Tables from: Sbidian_E, Chaimani_A, Afach_S, Doney_L, Dressler_C, Hua_C, Mazaud_C, Phan_C, Hughes_C, Riddle_D, Naldi_L, Garcia-Doval_I, LeCleach_L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD011535. DOI: 10.1002/14651858.CD011535.pub3 Pages 8-10
The treatments are presented in the same order as the SUCRA ranking results. This does not automatically mean statistically significant difference.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Any systemic treatment compared to placebo for chronic plaque psoriasis - PASI 90

Any systemic treatment compared to placebo for chronic plaque psoriasis - PASI 90[a]

Patient or population: people with chronic plaque psoriasis
Intervention: any systemic treatment
Comparison: placebo

Setting: Most trials recruited participants from hospital setting, but also in offices

Timescale: from 8 to 24 weeks after randomisation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	SUCRA[c]	№ of participants (studies)[d]	Certainty of the evidence (GRADE)	Comments
	Risk with placebo[b]	Risk with any systemic treatment					

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]The Psoriasis Area and Severity Index combines the assessment of the severity of lesions and the area affected into a single score in the range of 0 (no disease) to 72 (maximal disease); PASI 90: 90% improvement in the PASI.
[b]'Risk with placebo' is the median placebo-group risk value in the included studies for the assumed risk with placebo.

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	SUCRA[c]	C of participants (studies)[d]	Certainty of the evidence (GRADE)	Comments
	Risk with placebo[b]	Risk with any systemic treatment					
Infliximab	Moderate		RR 29.52 (19.94 to 43.70)	88.5	1651 (5 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to inconsistency: inconsistent loops of evidence
	15 per 1000	443 per 1000 (299 to 656)					
Ixekizumab	Moderate		RR 28.12 (23.17 to 34.12)	88.3	3268 (4 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to inconsistency: inconsistent loops of evidence
	15 per 1000	422 per 1000 (348 to 512)					
Risankizumab	Moderate		RR 27.67 (22.86 to 33.49)	87.5	1476 (4 RCTs)	⊕⊕⊕⊕ HIGH	-
	15 per 1000	415 per 1000 (343 to 502)					
Bimekizumab	Moderate		RR 58.64 (3.72 to 923.86)	83.5	250 (1 RCT)	⊕⊕⊖⊖ LOW	Downgraded by 2 levels due to imprecision: wide CI
	15 per 1000	880 per 1000 (56 to 1000)					
Guselkumab	Moderate		RR 25.84 (20.90 to 31.95)	81	1767 (5 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to risk of bias: 1 study contributing to this estimate at high risk of bias in selective reporting domain
	15 per 1000	388 per 1000 (313 to 479)					
Secukinumab	Moderate		RR 23.97 (20.03 to 28.70)	75.4	2895 (8 RCTs)	⊕⊕⊕⊕ HIGH	-
	15 per 1000	360 per 1000 (300 to 431)					
Brodalumab	Moderate		RR 21.96 (18.17 to 26.53)	68.7	4109 (5 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to risk of bias: 3 studies contributing to this estimate at high risk of bias in selective reporting domain
	15 per 1000	329 per 1000 (273 to 398)					
Adalimumab	Moderate		RR 17.82 (14.62 to 21.72)	58.1	3421 (9 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to inconsistency: inconsistent loops of evidence
	15 per 1000	267 per 1000 (219 to 326)					
Ustekinumab	Moderate		RR 17.17 (14.44 to 20.42)	55.6	4231 (9 RCTs)	⊕⊕⊕⊕ HIGH	-
	15 per 1000	258 per 1000 (217 to 306)					
Tildrakizumab	Moderate		RR 17.08 (12.93 to 22.56)	55.8	1903 (3 RCTs)	⊕⊕⊕⊕ HIGH	-
	15 per 1000	256 per 1000 (194 to 338)					
Oral tyrosine kinase 2 (TYK2) in-	Moderate		RR 13.99 (1.99 to 98.10)	51.5	267 (1 RCT)	⊕⊕⊖⊖ LOW	Downgraded by 2 levels due to imprecision: wide CI
	15 per 1000	210 per 1000 (30 to 1000)					
Certolizumab	Moderate		RR 12.11 (8.78 to 16.71)	42.5	1026 (4 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to risk of bias: 1 study at high risk of bias in blinding of participants and personnel (performance bias)
	15 per 1000	182 per 1000 (132 to 251)					
Ciclosporin	Moderate		RR 9.88 (5.45 to 17.91)	33.4	(0 RCTs)	⊕⊕⊖⊖ VERY LOW	Downgraded by 2 levels due to risk of bias/1 level due to imprecision: the studies contributing to this estimate are mostly at at high risk of bias, and wide CI
	15 per 1000	148 per 1000 (82 to 269)					
Etanercept	Moderate		RR 9.72 (8.12 to 11.63)	33	5650 (14 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to risk of bias: 1 study contributing to this estimate is at high
	15 per 1000 (122 to 174)	146 per 1000					risk of bias in blinding domains (blinding of participants and personnel (performance bias))
Methotrexate	Moderate		RR 9.78 (7.15 to 13.37)	32.9	318 (3 RCTs)	⊕⊕⊖⊖ LOW	Downgraded by 1 level due to inconsistency (inconsistent loops of evidence) and 1 level due to risk of bias: 1 study at high risk of bias in se- lective reporting (reporting bias)
	15 per 1000	147 per 1000 (107 to 201)					
Tofacitinib	Moderate		RR 8.19 (6.53 to 10.29)	23.4	3092 (5 RCTs)	⊕⊕⊖⊖ LOW	Downgraded by 2 level due to risk of bias: 2 studies at high risk of bias in incomplete outcome data domain and 1 study at high risk of bias in incomplete outcome data (attrition bias) domain
	15 per 1000	123 per 1000 (98 to 154)					
Apremilast	Moderate		RR 7.30 (4.26 to 12.51)	21.9	2029 (5 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to risk of bias: studies contributing to the estimates at high risk of bias in selective reporting domain
	15 per 1000	110 per 1000 (64 to 188)					
Fumaric acid	Moderate		RR 3.65 (2.49 to 5.36)	9.8	704 (1 RCT)	⊕⊕⊖⊖ VERY LOW	Downgraded by 2 levels due to risk of bias, and 1 level due to imprecision: the studies indirectly contributing to this estimate at high risk of bias in blinding domain, and only 1 study contributed to the direct estimation
	15 per 1000	55 per 1000 (37 to 80)					
Acitretin	Moderate		RR 2.13 (0.37 to 12.16)	8.1	(0 RCTs)	⊕⊕⊖⊖ VERY LOW	Downgraded by 2 levels due to imprecision (wide CI including 1) and 1 level due to risk of bias as the studies indirectly contributing to this estimate at high risk in blinding domain
	15 per 1000	32 per 1000 (6 to 182)					

Undesirable Effects

How substantial are the undesirable anticipated effects?

RESEARCH EVIDENCE

Tables from: Sbidian_E, Chaimani_A, Afach_S, Doney_L, Dressler_C, Hua_C, Mazaud_C, Phan_C, Hughes_C, Riddle_D, Naldi_L, Garcia-Doval_I, LeCleach_L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD011535. DOI: 10.1002/14651858.CD011535.pub3 Pages 8-10
The treatments are presented in the same order as the SUCRA ranking results. This does not automatically mean statistically significant difference.

Severe adverse events:

Summary of findings 2. Any systemic treatment compared to placebo for chronic plaque psoriasis - SAEs

Any systemic treatment compared to placebo for chronic plaque psoriasis - Serious adverse effects (SAEs)

Patient or population: people with chronic plaque psoriasis
Intervention: any systemic treatment
Comparison: placebo

Setting: Most trials recruited participants from hospital setting, but also in offices

Timescale: from 8 to 24 weeks after randomisation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	SUCRA[b]	Nº of participants (studies)[c]	Certainty of the evidence (GRADE)	Comments
	Risk with placebo[a]	Risk with any systemic treatment					

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]'Risk with placebo' is the median placebo-group risk value in the included studies for the assumed risk with placebo.
[b]SUCRA was expressed as a percentage between 0 (when a treatment is certain to be the worst) to 100% (when a treatment is certain to be the best).
[c]'Number of participants (studies)' is from the direct comparisons.

Outcomes	Anticipated absolute effects[a] (95% CI)		Relative effect (95% CI)	SUCRA[b]	C of participants (studies)[c]	Certainty of the evidence (GRADE)	Comments
	Risk with placebo[e]	Risk with any systemic treatment					
Methotrexate	Moderate		RR 0.43 (0.20 to 0.95)	87.6	319 (3 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI)
	17 per 1000	7 per 1000 (3 to 16)					
Bimekizumab	Moderate		RR 0.20 (0.01 to 3.16)	84.3	250 (1 RCT)	⊕⊕⊕⊖ LOW	Downgraded by 2 levels due to imprecision (wide CI including 1)
	17 per 1000	3 per 1000 (0 to 54)					
Risankizumab	Moderate		RR 0.60 (0.37 to 0.96)	79.9	1476 (4 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due imprecision (wide CI)
	17 per 1000	10 per 1000 (6 to 16)					
Certolizumab	Moderate		RR 0.74 (0.31 to 1.75)	62.4	1026 (4 RCTs)	⊕⊕⊕⊖ LOW	Downgraded by 1 level due to risk of bias (1 study at high risk of bias in blinding of participants and personnel (performance bias)) and 1 level due to imprecision (wide CIs including 1)
	17 per 1000	13 per 1000 (5 to 30)					
Oral Tyrosine kinase 2 (TYK2) inhibitor	Moderate		RR 0.61 (0.06 to 5.71)	61.6	267 (1 RCT)	⊕⊕⊕⊖ LOW	Downgraded by 2 levels due to imprecision (wide CI including 1)
	17 per 1000	10 per 1000 (1 to 97)					
Tildrakizumab	Moderate		RR 0.84 (0.39 to 1.83)	54.6	1904 (3 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	14 per 1000 (7 to 31)					
Apremilast	Moderate		RR 0.86 (0.48 to 1.51)	54.5	2290 (6 RCTs)	⊕⊕⊕⊖ LOW	Downgraded by 1 level due to risk of bias and 1 level due to imprecision due to wide CI including 1
	17 per 1000	15 per 1000 (8 to 26)					
Ustekinumab	Moderate		RR 0.89 (0.63 to 1.27)	52.7	4553 (10 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	15 per 1000 (11 to 22)					
Etanercept	Moderate		RR 0.89 (0.61 to 1.31)	52.6	4265 (13 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CIs including 1)
	17 per 1000	15 per 1000 (10 to 22)					
Fumaric acid esters	Moderate		RR 0.98 (0.50 to 1.94)	43.5	704 (1 RCT)	⊕⊕⊕⊖ VERY LOW	Reasons for downgrading by 2 level due to risk of bias and 1 level due to imprecision, and to wide CI including 1
	17 per 1000	17 per 1000 (9 to 33)					
Guselkumab	Moderate		RR 0.98 (0.54 to 1.79)	43.2	1767 (5 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	17 per 1000 (9 to 30)					
Adalimumab	Moderate		RR 0.98 (0.65 to 1.49)	42.6	3485 (10 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	17 per 1000 (11 to 25)					
Tofacitinib	Moderate		RR 1.01 (0.57 to 1.77)	41.2	3122 (7 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	17 per 1000 (10 to 30)					
Brodalumab	Moderate		RR 1.04 (0.62 to 1.73)	38.4	4109 (5 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	18 per 1000 (11 to 29)					
Infliximab	Moderate		RR 1.11 (0.59 to 2.07)	33.9	1678 (6 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	19 per 1000 (10 to 35)					
Ixekizumab	Moderate		RR 1.09 (0.69 to 1.73)	33	3268 (4 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	16 per 1000 (10 to 26)					
Ciclosporin	Moderate		RR 1.47 (0.19 to 11.22)	32	(0 RCTs)	⊕⊕⊕⊖ VERY LOW	Downgraded by 2 levels due to risk of bias/1 level due to imprecision (the studies contributing to this estimate are mostly at at high risk of bias), and wide CI including 1
	17 per 1000	25 per 1000 (3 to 191)					
Acitretin	Moderate		RR 1.53 (0.19 to 12.56)	31.2	(0 RCTs)	⊕⊕⊕⊖ VERY LOW	Downgraded by 2 levels due to imprecision (wide CI including 1) and 1 level due to risk of bias as the studies indirectly contributing to this estimate at high risk in blinding domain
	17 per 1000	26 per 1000 (3 to 214)					
Secukinumab	Moderate		RR 1.12 (0.74 to 1.70)	30.4	2904 (8 RCTs)	⊕⊕⊕⊖ MODERATE	Downgraded by 1 level due to imprecision (wide CI including 1)
	17 per 1000	19 per 1000 (13 to 29)					

Certainty of evidence

What is the overall certainty of the evidence of effects?

Table below: Study bias distribution for PASI 90 using CINeMA (table provided by Emilie Sbidian, thank you)

Sbidian_E, Chaimani_A, Afach_S, Doney_L, Dressler_C, Hua_C, Mazaud_C, Phan_C, Hughes_C, Riddle_D, Naldi_L, Garcia-Doval_I, LeCleach_L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD011535. DOI: 10.1002/14651858.CD011535.pub3 Pages 560 ff

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
ACI:ETA	2	Major concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Low
ADA:GUSEL	3	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ADA:MTX	1	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:PBO	9	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ADA:RISAN	1	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
APRE:ETA	1	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
APRE:PBO	5	No concerns	Undetected	Some concerns	No concerns	No concerns	No concerns	Moderate
BIME:PBO	1	No concerns	Undetected	Some concerns	No concerns	No concerns	Some concerns	Low
BRODA:PBO	5	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
BRODA:USK	2	Some concerns	Undetected	No concerns	No concerns	Some concerns	No concerns	Moderate
CERTO:ETA	1	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
CERTO:PBO	4	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
CICLO:MTX	2	Major concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Very low
ETA:IFX	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
ETA:IXE	2	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ETA:PBO	14	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ETA:SECU	1	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ETA:TILDRA	1	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ETA:TOFA	1	No concerns	Undetected	No concerns	No concerns	Some concerns	No concerns	Moderate
ETA:USK	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
FUM:GUSEL	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
FUM:IXE	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
FUM:MTX	2	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
FUM:PBO	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
FUM:SECU	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
GUSEL:PBO	5	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
IFX:MTX	1	Major concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Low
IFX:PBO	5	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
IXE:MTX	1	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
IXE:PBO	4	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
IXE:USK	1	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
MTX:PBO	3	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
PBO:RISAN	4	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
PBO:SECU	8	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
PBO:TILDRA	3	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
PBO:TOFA	5	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
PBO:TYK2	1	No concerns	Undetected	Some concerns	No concerns	No concerns	Some concerns	Moderate
PBO:USK	9	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
RISAN:USK	3	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
SECU:USK	2	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ACI:ADA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:APRE	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
ACI:BIME	0	Some concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
ACI:BRODA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:CERTO	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ACI:CICLO	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ACI:FUM	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
ACI:GUSEL	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:IFX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
ACI:IXE	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:MTX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ACI:PBO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
ACI:RISAN	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:SECU	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:TILDRA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ACI:TOFA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
ACI:TYK2	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
ACI:USK	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:APRE	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:BIME	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
ADA:BRODA	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ADA:CERTO	0	No concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ADA:CICLO	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ADA:ETA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:FUM	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:IFX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
ADA:IXE	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:SECU	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:TILDRA	0	No concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
ADA:TOFA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ADA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
ADA:USK	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:BIME	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
APRE:BRODA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:CERTO	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
APRE:CICLO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
APRE:FUM	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:GUSEL	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:IFX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
APRE:IXE	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:MTX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
APRE:RISAN	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:SECU	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:TILDRA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
APRE:TOFA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
APRE:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
APRE:USK	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BIME:BRODA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:CERTO	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:CICLO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:ETA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
BIME:FUM	0	Some concerns	Undetected	Some concerns	Some concerns	No concerns	Some concerns	Low
BIME:GUSEL	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:IFX	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:IXE	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:MTX	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:RISAN	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:SECU	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
BIME:TOFA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
BIME:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
BIME:USK	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
BRODA:CERTO	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
BRODA:CICLO	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BRODA:ETA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BRODA:FUM	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BRODA:GUSEL	0	No concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
BRODA:IFX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Low
BRODA:IXE	0	Some concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
BRODA:MTX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BRODA:RISAN	0	Some concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
BRODA:SECU	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BRODA:TILDRA	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
BRODA:TOFA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
BRODA:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
CERTO:CICLO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
CERTO:FUM	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CERTO:GUSEL	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CERTO:IFX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
CERTO:IXE	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CERTO:MTX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
CERTO:RISAN	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CERTO:SECU	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CERTO:TILDRA	0	No concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
CERTO:TOFA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CERTO:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
CERTO:USK	0	Some concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
CICLO:ETA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
CICLO:FUM	0	Major concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
CICLO:GUSEL	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CICLO:IFX	0	Major concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
CICLO:IXE	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CICLO:PBO	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CICLO:RISAN	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
CICLO:SECU	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
CICLO:TILDRA	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
CICLO:TOFA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
CICLO:TYK2	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
CICLO:USK	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
ETA:FUM	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
ETA:GUSEL	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ETA:MTX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ETA:RISAN	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
ETA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
FUM:IFX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
FUM:RISAN	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
FUM:TILDRA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
FUM:TOFA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
FUM:TYK2	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Very low
FUM:USK	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
GUSEL:IFX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Low
GUSEL:IXE	0	No concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
GUSEL:MTX	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
GUSEL:RISAN	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
GUSEL:SECU	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
GUSEL:TILDRA	0	No concerns	Undetected	No concerns	No concerns	Some concerns	Some concerns	Moderate
GUSEL:TOFA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
GUSEL:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
GUSEL:USK	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
IFX:IXE	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Low
IFX:RISAN	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Low
IFX:SECU	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Low
IFX:TILDRA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
IFX:TOFA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
IFX:TYK2	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
IFX:USK	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Low
IXE:RISAN	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
IXE:SECU	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
IXE:TILDRA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
IXE:TOFA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
IXE:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
MTX:RISAN	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
MTX:SECU	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
MTX:TILDRA	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
MTX:TOFA	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
MTX:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
MTX:USK	0	Some concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
RISAN:SECU	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
RISAN:TILDRA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
RISAN:TOFA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
RISAN:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
SECU:TILDRA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
SECU:TOFA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
SECU:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
TILDRA:TOFA	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
TILDRA:TYK2	0	No concerns	Undetected	No concerns	Major concerns	No concerns	Some concerns	Low
TILDRA:USK	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
TOFA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low
TOFA:USK	0	No concerns	Undetected	No concerns	No concerns	No concerns	Some concerns	Moderate
TYK2:USK	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	Some concerns	Low

Table below: Study bias distribution for serious adverse events using CINeMA (table provided by Emilie Sbidian, thank you)

Sbidian_E, Chaimani_A, Afach_S, Doney_L, Dressler_C, Hua_C, Mazaud_C, Phan_C, Hughes_C, Riddle_D, Naldi_L, Garcia-Doval_I, LeCleach_L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD011535. DOI: 10.1002/14651858.CD011535.pub3 pages 571 ff

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
ACI:ETA	3	Major concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Very low
ADA:GUSEL	3	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ADA:MTX	1	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ADA:PBO	10	No concerns	Undetected	Some concerns	Some concerns	Some concerns	Major concerns	Very low
ADA:RISAN	1	No concerns	Undetected	No concerns	Some concerns	No concerns	Some concerns	Moderate
APRE:ETA	1	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:PBO	6	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:PBO	1	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BRODA:PBO	5	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:USK	2	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:ETA	1	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:PBO	4	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CICLO:MTX	2	Major concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Very low
CICLO:PBO	1	Major concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Very low
ETA:IFX	1	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ETA:IXE	2	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ETA:PBO	13	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ETA:SECU	1	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ETA:TILDRA	1	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ETA:TOFA	1	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ETA:USK	1	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
FUM:GUSEL	1	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
FUM:IXE	1	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
FUM:MTX	2	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
FUM:PBO	1	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
FUM:SECU	1	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low

GUSEL:PBO	5	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
IFX:MTX	1	Major concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Low
IFX:PBO	7	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IXE:MTX	1	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
IXE:PBO	4	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
IXE:USK	1	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
MTX:PBO	3	Some concerns	Undetected	Some concerns	No concerns	No concerns	No concerns	Moderate
PBO:RISAN	4	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
PBO:SECU	8	No concerns	Undetected	Some concerns	Some concerns	No concerns	No concerns	Moderate
PBO:TILDRA	3	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
PBO:TOFA	7	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
PBO:TYK2	1	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
PBO:USK	10	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
RISAN:USK	3	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
SECU:USK	2	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ACI:ADA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:APRE	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:BIME	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:BRODA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:CERTO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:CICLO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:FUM	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:GUSEL	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:IFX	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:IXE	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:MTX	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:PBO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:RISAN	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:SECU	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:TILDRA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:TOFA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ACI:TYK2	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low

ACI:USK	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ADA:APRE	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:BIME	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:BRODA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ADA:CERTO	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:CICLO	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:ETA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ADA:FUM	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:IFX	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:IXE	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ADA:SECU	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ADA:TOFA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ADA:USK	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
APRE:BIME	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:BRODA	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:CERTO	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:CICLO	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:FUM	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:GUSEL	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:IFX	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:IXE	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:MTX	0	Some concerns	Undetected	Some concerns	Some concerns	No concerns	No concerns	Moderate
APRE:RISAN	0	No concerns	Undetected	Some concerns	Some concerns	No concerns	No concerns	Moderate
APRE:SECU	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:TILDRA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:TOFA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
APRE:USK	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low

BIME:BRODA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:CERTO	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:CICLO	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:ETA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:FUM	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:GUSEL	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:IFX	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:IXE	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:MTX	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:RISAN	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:SECU	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:TILDRA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:TOFA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BIME:USK	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BRODA:CERTO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:CICLO	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:ETA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:FUM	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:GUSEL	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:IFX	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
BRODA:IXE	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:MTX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
BRODA:RISAN	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
BRODA:SECU	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:TOFA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
BRODA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CERTO:CICLO	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CERTO:FUM	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low

CERTO:GUSEL	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:IFX	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CERTO:IXE	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:MTX	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:RISAN	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:SECU	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CERTO:TOFA	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CERTO:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CERTO:USK	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CICLO:ETA	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CICLO:FUM	0	Major concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Very low
CICLO:GUSEL	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CICLO:IFX	0	Major concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Very low
CICLO:IXE	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CICLO:RISAN	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CICLO:SECU	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CICLO:TILDRA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
CICLO:TOFA	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CICLO:TYK2	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
CICLO:USK	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
ETA:FUM	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ETA:GUSEL	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
ETA:MTX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ETA:RISAN	0	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
ETA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
FUM:IFX	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
FUM:RISAN	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
FUM:TILDRA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
FUM:TOFA	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low

FUM:TYK2	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
FUM:USK	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
GUSEL:IFX	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
GUSEL:IXE	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
GUSEL:MTX	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
GUSEL:RISAN	0	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
GUSEL:SECU	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
GUSEL:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
GUSEL:TOFA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
GUSEL:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
GUSEL:USK	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
IFX:IXE	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IFX:RISAN	0	No concerns	Undetected	Some concerns	Some concerns	No concerns	No concerns	Moderate
IFX:SECU	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IFX:TILDRA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IFX:TOFA	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IFX:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IFX:USK	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
IXE:RISAN	0	No concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	High
IXE:SECU	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
IXE:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
IXE:TOFA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
IXE:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
MTX:RISAN	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
MTX:SECU	0	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	Moderate
MTX:TILDRA	0	Some concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
MTX:TOFA	0	Some concerns	Undetected	Some concerns	Some concerns	No concerns	No concerns	Moderate
MTX:TYK2	0	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
MTX:USK	0	Some concerns	Undetected	No concerns	Some concerns	No concerns	No concerns	Moderate
RISAN:SECU	0	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
RISAN:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
RISAN:TOFA	0	No concerns	Undetected	Some concerns	Some concerns	No concerns	No concerns	Moderate

RISAN:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
SECU:TILDRA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
SECU:TOFA	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
SECU:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
TILDRA:TOFA	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
TILDRA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
TILDRA:USK	0	No concerns	Undetected	No concerns	Major concerns	No concerns	No concerns	Low
TOFA:TYK2	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
TOFA:USK	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low
TYK2:USK	0	No concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Low

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

RESEARCH EVIDENCE

Several different ways of **classifying the severity of psoriasis** exist.

According to a European consensus from 2011 (5), psoriasis is classified as:

- Moderate-to-severe disease: (PASI > 10 OR body surface area [BSA] > 10) AND DLQI > 10
- Mild psoriasis: PASI ≤ 10 AND BSA ≤ 10 AND DLQI ≤ 10.

In 2017, Llamas-Velasco et al suggested the following psoriasis severity definitions(6):

- mild, PASI<7 and DLQI<7;
- moderate, PASI=7-15 and DLQI=5-15 (classified as severe when difficult-to-treat sites are affected or when there is a significant psychosocial impact);
- severe, PASI >15, independently of the DLQI score."

The International Psoriasis Council Board Members and Councillors re-categorized psoriasis in 2020 as follows (page 121, Strober et al 2020 (7):

„Psoriasis patients should be classified as candidates for topical therapy or candidates for systemic therapy. The latter are patients who meet at least 1 of the following criteria:

1. BSA >10%
2. Disease involving special areas
3. Failure of topical therapy"

Taking into account the impact of important psoriasis characteristics from the patient's perspective criteria have been defined, which upgrade mild disease to moderate-to-severe when present. These include a major involvement of visible areas, major involvement of the scalp, involvement of genitals, onycholysis or onychodystrophy of at least two fingernails, presence of itch leading to scratching and the presence of recalcitrant plaques (8).

Since the European consensus group meeting, considerable process has been made concerning the development of new treatment options for psoriasis. They had, for example, defined treatment success during induction treatment as PASI75 (5).

In many countries, higher **treatment goals** (e.g. PASI 90) are aimed for. In addition, the focus has shifted away from a percentage reduction towards a targeted final outcome (e.g. PASI < 2, DLQI < 2 or PGA clear or almost clear (9).

- Patients are first interested in safety followed by efficacy of biologic treatment, with some variations (10)
- Sociodemographic factors play a role; access and delivery are important attributes

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

RESEARCH EVIDENCE

Tables/figures from: Sbidian_E, Chaimani_A, Afach_S, Doney_L, Dressler_C, Hua_C, Mazaud_C, Phan_C, Hughes_C, Riddle_D, Naldi_L, Garcia-Doval_I, LeCleach_L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD011535. DOI: 10.1002/14651858.CD011535.pub3. pages 38 and page 44

Figure 7: PASI 90 (left/bottom) and SAEs (right/top) .(assessment from 8 to 24 weeks after randomisation). **Drugs are reported in order of primary benefit ranking**. Each cell contains the risk ratio (RR) and 95% confidence interval for the two primary outcomes (PASI 90 and SAEs)) [Copyright © 2020 The Cochrane Collaboration]

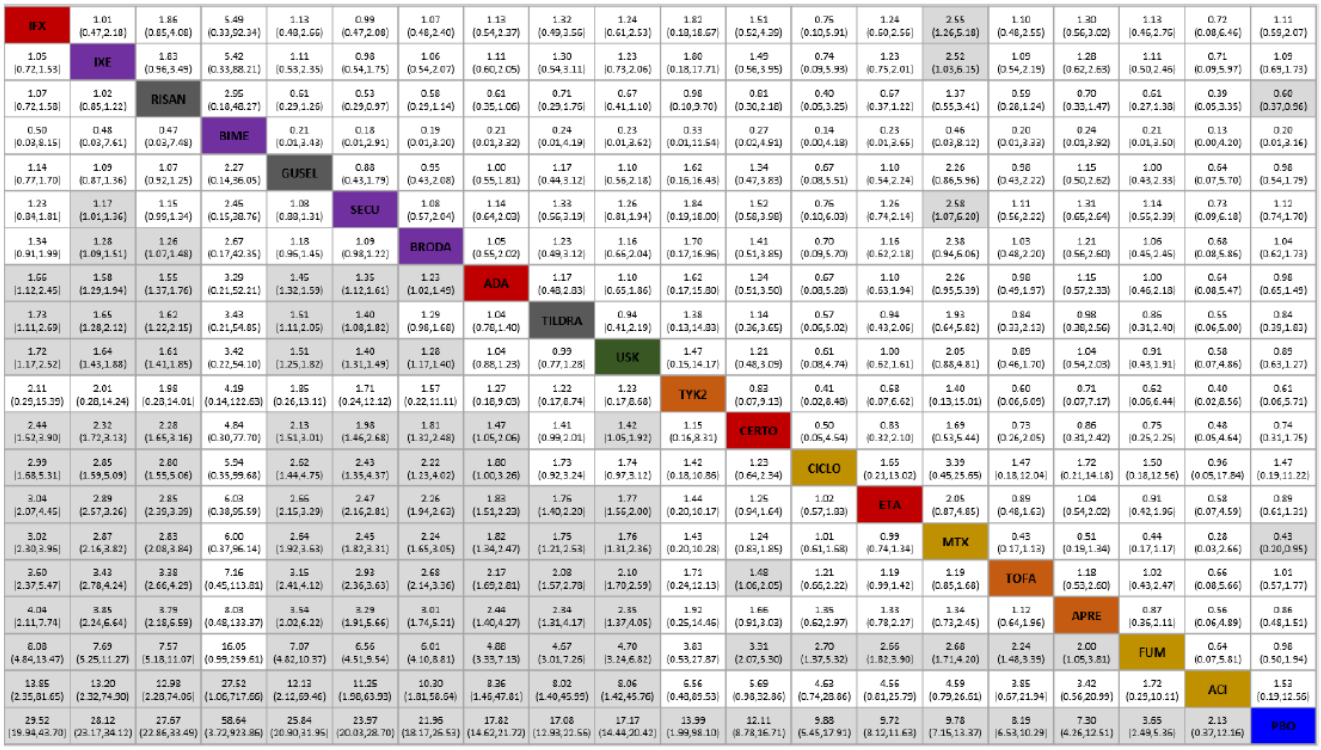
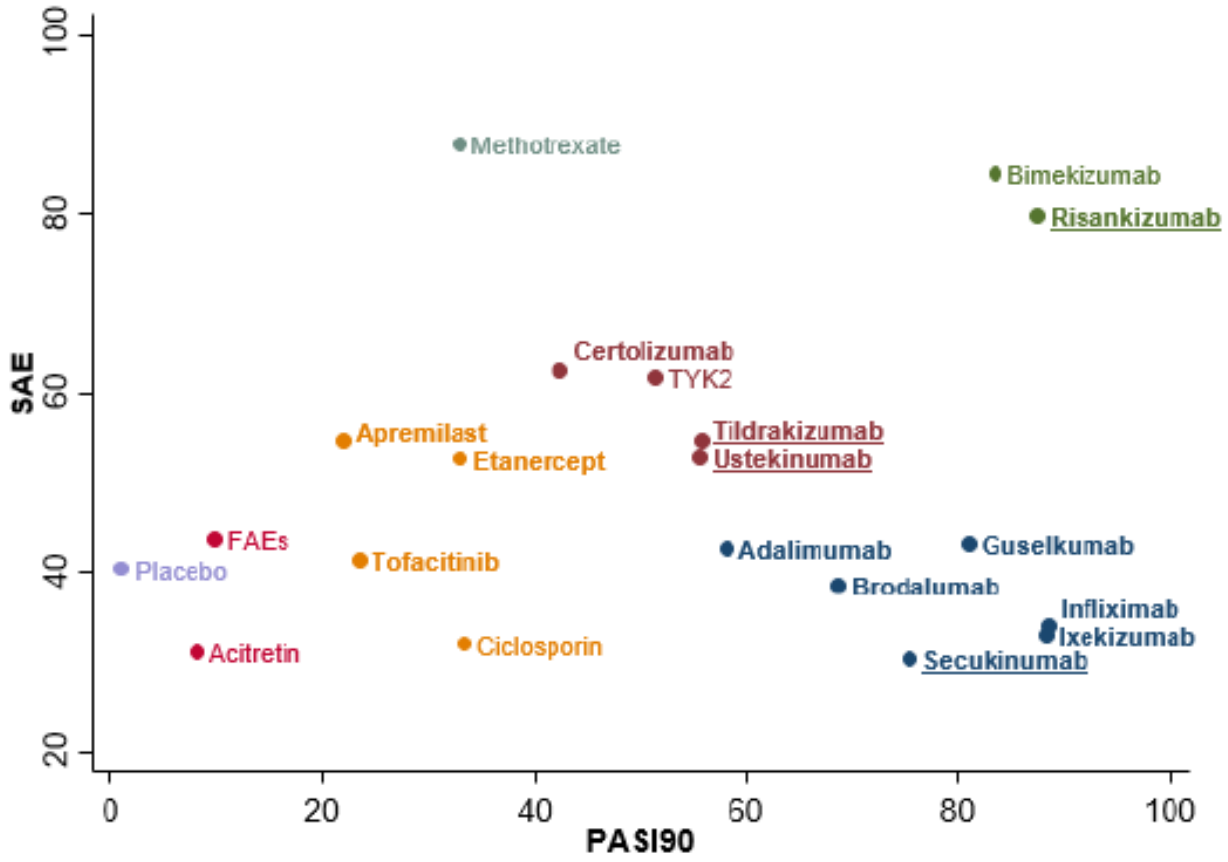


Figure 12: Ranking Plot (efficacy x-axis, safety y-axis). Optimal treatment should be characterised by both high efficacy and acceptability (upper right corner).) [Copyright © 2020 The Cochrane Collaboration]



Equity

What would be the impact on health equity?

RESEARCH EVIDENCE

- Costs remain barrier to prescribing biologics (11)
- In addition, national regulations and reimbursement situation need to be taken into consideration and treatment algorithms need to be adapted to regional or national specific circumstances.

Acceptability

Is the intervention acceptable to key stakeholders?

RESEARCH EVIDENCE

- Patients are first interested in safety followed by efficacy of treatment, with some variations (10)
- Sociodemographic factors play a role; access and delivery are important attributes

Recommendations

For main recommendations and flow chart, see guideline document

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 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.

Subgroup considerations

We considered the evidence alongside further research for patients with comorbidities and special patient populations .

Implementation considerations

The main barrier to implementation may be the national/local limitation to drug reimbursement, making the prescription of costly treatments such as the biologics and small molecules difficult.

Monitoring and evaluation

Monitoring and evaluation is to be done on national levels.

- Change in practice performance
- Change in health outcomes
- Change in end-user knowledge and understanding

As an example for national monitoring and evaluation strategies, see BAD (12) or for an example of a cross sectional survey about psoriasis patient care (13)

Monitoring over two years following publication(done by EuroGuiDerm Team):

- Number of accesses and/or downloads from the EDF website
- Altmetric-Score of the journal publication
- Number of Web of Science citations
- Number of countries which adopted (translated the guideline as is, without change of content); this is presented separately for European countries, regions and non-European countries
- Number of countries which adapted the guideline (used parts of the guideline, or some recommendations); this is presented separately for European countries, regions and non-European countries

Research priorities

- -Which are the predictors for treatment success or the occurrence of adverse events?
- -What is the role of therapeutic drug monitoring?
- -When should a treatment be stopped in case of clearance?
- -Which treatments can be combined safely and lead to improved efficacy?
- What is the most suitable treatment option in given comorbid situations?

Appendix 2 Evidence to Decision Framework psoriatic arthritis

Psoriatic arthritis: Update of a systematic review on the systemic treatment of psoriatic arthritis

We updated existing systematic reviews from Dressler et al. (14) and Pham et al.(15) , which had been developed by the same working group in parallel.

For the guideline, the recommendations focus on treatment options suitable and licensed for both conditions as the target group of this guideline are dermatologists, treating patients with moderate to severe psoriasis. The systematic review, however, was done for all treatment options licenced for psoriatic arthritis.

First we report the evidence to decision framework, thereafter the details of the systematic review update.

Evidence to decision framework

For patients with moderate to severe plaque type psoriasis and concomitant psoriatic arthritis, what are the clinical efficacy, safety and tolerability of approved (for both plaque type psoriasis and psoriatic arthritis) conventionals (methotrexate), biologics (adalimumab, brodalumab, certolizumab pegol, etanercept, infliximab, ixekizumab, secukinumab, ustekinumab) or small molecules (apremilast) compared with each other or with placebo?	
POPULATION:	Patients with moderate to severe psoriasis vulgaris and concomitant psoriatic arthritis
INTERVENTION:	Considered for the guideline recommendation(s): only systemic treatments approved for both plaque type psoriasis and psoriatic arthritis • conventional synthetic disease modifying anti rheumatic drugs (csDMARDs): MTX, • targeted synthetic (ts)DMARDS: apremilast, • biological (b)DMARDs: ADA, CZP, ETA, INF, UST, IXE, SEC
COMPARISON:	One of the above or placebo
MAIN OUTCOMES:	- Efficacy outcomes: 20% improvement in the mACR criteria - Safety outcomes: proportion of patients with at least one AE
SETTING:	- Region: Europe (study inclusion not limited to studies done in Europe) - Setting: clinical and practice (private and public) dermatologists
PERSPECTIVE:	- Population perspective
BACKGROUND:	- Concomitant psoriatic arthritis is frequent in patients with moderate to severe plaque type psoriasis. - Several new treatments have been developed and approved since the last version of the guideline, additional evidence is available as further studies have been performed and published. - Access to specialist care is limited and in many countries long waiting periods are required for specialist appointments, appropriate treatment choice from dermatologists for patients with concomitant psoriatic arthritis needs to be ensured. - It is important to note that specific subtypes of psoriatic arthritis exist (e.g. peripheral, axial, enthesitis, dactylitis) and that response rates to drugs may vary based on the subtype. Evidence synthesis updated based on Dressler et al and Pham et al.(14, 15)

CONFLICT OF INTERESTS:	Less than 50% of the guideline development committee declared to have personal-financial conflicts of interests (see Methods & Evidence report of this guideline).

Needs Assessment

RESEARCH EVIDENCE

- Access to specialist care is limited and in many countries long waiting periods are required for specialist appointments, appropriate treatment choice from dermatologists for patients with concomitant psoriatic arthritis needs to be ensured.

Desirable Effects

How substantial are the desirable anticipated effects?

RESEARCH EVIDENCE

For details of systematic review, see below.
Psoriatic arthritis: Update of a systematic review on the systemic treatment of psoriatic arthritis

Summary of the results for drugs approved for psoriasis of the skin and psoriatic arthritis (Dressler et al (14) updated, below)

	Patients achieving ACR20		
	RR	95% CI	Quality of the Evidence (GRADE)
Head-to-head comparisons			
ETA 50mg + MTX vs. MTX 20mg QW	1.28	1.11 to 1.48	LOW
INF 5mg/kg W 0,2,6,14 + MTX vs. MTX 15mg QW	1.40	1.07 to 1.84	VERY LOW
IXE 80mg Q2W vs. ADA 40mg Q2W	1.08	0.86 to 1.36	LOW
IXE 80mg Q4W vs. ADA 40mg Q2W	0.96	0.86 to 1.06	LOW
Placebo comparisons			
ADA 40mg EOW vs. PBO	3.35	2.24 to 4.99	MODERATE
APR 30mg BID vs. PBO	1.94	1.59 to 2.38	MODERATE
APR 20mg BID vs PBO	1.86	1.49 to 2.31	MODERATE
CZP 400mg Q4W vs. PBO	2.36	1.68 to 3.31	MODERATE
CZP 200mg Q2W vs. PBO	2.71	1.95 to 3.76	MODERATE
ETA 25mg BIW vs. PBO	4.05	2.56 to 6.40	LOW
INF 5mg/kg W0,2,6,14vs. PBO	4.38	2.24 to 8.56	MODERATE

IXE 80mg Q2W vs. PBO	2.21	1.71 to 2.86	MODERATE
IXE 80mg Q4W vs. PBO	2.25	1.59 to 3.18	MODERATE
MTX 7.5mg QW vs. PBO	1.82	0.97 to 3.40	LOW
SEC 150mg Q4W vs. PBO	2.44	2.10 to 2.84	HIGH
SEC 150mg Q4W+ LD vs. PBO	2.06	1.70 to 2.49	HIGH
SEC 300mg Q4W + LD vs. PBO	2.28	1.87 to 2.80	MODERATE
UST 45mg W0,4, Q12W vs PBO	1.95	1.52 to 2.50	HIGH
UST 90mg W0,4, Q12W vs PBO	2.26	1.80 to 2.82	MODERATE

One study (Gottlieb et al. 2009) reported induction dose of QW (weeks 0-3). Abbreviations: ACR20 = 20% improvement in American College of Rheumatology response criteria; RR = risk ratio; 95% CI = 95% confidence interval; ETA = Etanercept; MTX = Methotrexate; mg = milligrams; QW= once a week; INF = Infliximab; kg = kilograms IXE = Ixekizumab; ADA = Adalimumab; Q2W = once every 2 weeks; EOW = every other week; PBO = placebo; APR = Apremilast; BID = twice a day; CZP = Certolizumab Pegol; Q4W = once every 4 weeks; BIW = twice a week; W = week; Sec = Secukinumab; LD = loading dose; UST = Ustekinumab; Q12W = every 12 weeks.

Effects with regard to ACR 20 response from included treatment options versus placebo were considered as relevant. Difference in the effects of anti – TNF antagonists versus IL 17 antagonists with regard to ACR 20 were considered as irrelevant or of minor importance (indirect comparisons with relevant methodological limitations).

Undesirable Effects

How substantial are the undesirable anticipated effects?

RESEARCH EVIDENCE

For details of systematic review, see below.
Psoriatic arthritis: Update of a systematic review on the systemic treatment of psoriatic arthritis

Summary of the results for drugs approved for psoriasis of the skin and psoriatic arthritis (Dressler et al (14) updated, below)

	Patients with at least one adverse event		
	RR	95% CI	Quality of the Evidence (GRADE)
Head-to-head comparisons			
ETA 50mg + MTX vs. MTX 20mg QW	1.01	0.92 to 1.11	MODERATE
INF 5mg/kg W 0, 2, 6, 14 + MTX vs. MTX 15mg QW. MTX 15mg QW	1.65	1.08 to 2.52	VERY LOW
IXE 80mg Q2W vs. ADA 40mg Q2W	1.02	0.83 to 1.25	MODERATE
IXE 80mg Q4W vs. ADA 40mg Q2W	1.14	1.01 to 1.28	VERY LOW
Placebo comparisons			
ADA 40mg EOW vs. PBO	0.67	0.50 to 0.89	VERY LOW

APR 30mg BID vs. PBO	1.24	1.12 to 1.36	LOW
APR 20mg BID vs PBO	1.27	1.15 to1.41	LOW
CZP 400mg Q4W vs. PBO	1.05	0.90 to 1.23	MODERATE
CZP 200mg Q2W vs. PBO	1.01	0.86 to 1.19	MODERATE
ETA 25mg BIW vs. PBO	n.d.		
INF 5mg/kg W 0, 2, 6, 14 vs. PBO	1.13	0.87 to 1.47	LOW
IXE 80mg Q2W vs. PBO	1.39	1.09 to 1.78	LOW
IXE 80mg Q4W vs. PBO	1.41	1.10 to 1.79	LOW
MTX 7.5mg QW vs. PBO	n.d.		
SEC 150mg Q4W vs. PBO	1.03	0.95 to 1.12	HIGH
SEC 150mg Q4W **+ LD vs. PBO**	1.01	0.89 to 1.15	MODERATE
SEC 300mg Q4W **+ LD vs. PBO**	1.02	0.89 to 1.16	MODERATE
UST 45mg W 0, 4 and Q12W vs PBO	n.d.		
UST 90mg W 0, 4 and Q12W* **vs PBO**	0.96	0.75 to1.24	VERY LOW

*One study (Gottlieb et al. 2009) reported induction dose of QW (weeks 0-3). Abbreviations: RR = risk ratio; 95% CI = 95% confidence interval; ETA = Etanercept; MTX = Methotrexate; mg = milligrams; QW= once a week; INF = Infliximab; kg = kilograms IXE = Ixekizumab; ADA = Adalimumab; Q2W = once every 2 weeks; EOW = every other week; PBO = placebo; APR = Apremilast; BID = twice a day; CZP = Certolizumab Pegol; Q4W = once every 4 weeks; BIW = twice a week; W = week; Sec = Secukinumab; LD = loading dose; UST = Ustekinumab; Q12W = every 12 weeks.

Assessment of undesirable effects was limited due to limited direct comparability of safety results and safety reporting. The assessments of undesirable effect with regard to the available data on "Patients with at least one adverse event" were considered not to be specific enough to guide general treatment recommendations. A treatment safety profile needs to be individually matched to a specific patient (see also other chapters on comorbid situations).

Certainty of evidence

What is the overall certainty of the evidence of effects?

	ACR20 - induction Certainty assessment							Adverse Events - induction Certainty assessment						
Comparison	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Head-to-head comparisons:														

Etanercept 50mg+ MTX vs. Methotrexate 20 mg QW +PBO	1	RCT	not serious	not serious	serious[a]	serious[b]	none	1	RCT	not serious	not serious	serious[a]	not serious	none
a. only 1 study available; b. 95% confidence limit crosses MID threshold (1.25) uncertain whether it is clinical important														
Infliximab 5mg/kg + MTX 15mg/w vs Methotrexate 15mg/w	1	RCT	serious[a]	serious[b]	not serious	serious[c]	none	1	RCT	serious[a]	serious[b]	not serious	serious[d]	none
a. open-label RCT; small sample size; b. only one study available; c. 95% confidence limit crosses MID (1.25); statistically significant but clinical importance uncertain; d 95% confidence limit crosses line of appreciable harm (1.25); statistically significant but clinical importance uncertain														
Ixekizumab 80mg Q2W vs Adalimumab 40mg Q2W	1	RCT	not serious	serious[a]	not serious	serious[b]	none	1	RCT	not serious	serious[a]	not serious	not serious	none
a. only one study available; b. 95% CI crosses line of no effect and MID threshold (1.25); uncertain whether there is any difference														
Ixekizumab 80mg Q4W vs. Adalimumab	1	RCT	very serious[a]	not serious	serious[b]	not serious	none	1	RCT	very serious[a]	not serious	serious[b]	serious[c]	none
a. Open label RCT (RoB= high for allocation concealment and blinding); b. Only one study; c. 95% confidence limit crosses MID threshold (1.25); statistically significant but clinical importance uncertain														
Placebo comparisons:														
Adalimumab 40mg EOW vs. placebo	2	RCT	serious[a]	not serious	not serious	not serious	none	1	RCT	serious[b]	not serious	serious[c]	serious[d]	none
a. unclear allocation concealment, randomization method and blinding (RoB = unclear 2/2), b. unclear blinding of personnel and patients (RoB=unclear 1/1) ,c. Only one study ,d. 95% confidence limit crosses lines of MID (0.75); uncertain whether it is clinical significant														
Apremilast 30mg BID vs. placebo	5	RCT	serious[a]	not serious	not serious	not serious	none	5	RCT	serious[a]	not serious	not serious	serious[b]	none
a. unclear allocation concealment and randomization methods in 4 of 5 RCTs (ROB = unclear 5/5 RCTs);b. 95% confidence limit crosses MID threshold (1.25); statistically significant but clinical importance uncertain														
Apremilast 20mg BID vs. placebo	4	RCT	serious[a]	not serious	not serious	not serious	none	4	RCT	serious[a]	not serious	not serious	serious[b]	none
a. unclear allocation concealment and randomization methods in 3 of 4 RCTs (RoB=unclear 4/4); b. 95% confidence limit crosses MID threshold (1.25); statistically significant but clinical importance uncertain														
Certolizumab pegol 400mg Q4W vs placebo	1	RCT	not serious	serious[a]	not serious	not serious	none	1	RCT	not serious	serious[a]	not serious	not serious	none
a. only one study available														
Certolizumab pegol 200mg Q2W vs placebo	1	RCT	not serious	serious[a]	not serious	not serious	none	1	RCT	not serious	serious[a]	not serious	not serious	none
a. only one study available														
Etanercept 25mg BIW vs. placebo	2	RCT	very serious[a]	not serious	not serious	not serious	none	no data	no data	no data	no data	no data	no data	no data
a. unclear randomization and allocation concealment, and high incomplete outcome data (RoB= unclear 1/2 and high 1/2)														
Infliximab 5mg/kg W0, 2, 6, 14 vs placebo	2	RCT	not serious	not serious	serious[a]	not serious	none	1	RCT	not serious	serious[b]	not serious	serious[c]	none
a. data was pooled across 16 and 24 weeks (IMPACT: 16weeks, IMPACT2: 24 weeks, the latter included early escape options and hence more NRI for early escapers); b. only one study available; c. 95% confidence limit crossed lines of no effect and appreciable harm; uncertain whether there is any difference														
Ixekizumab 80mg Q2W vs placebo	2	RCT	not serious	not serious	serious[a]	not serious	none	1	RCT	not serious	serious[b]	not serious	serious[c]	none
a. different inclusion criteria (bDMARD naive vs. non-responder to 1 or 2 anti TNF alpha); b. only one study available; c. 95% confidence limit crosses MID (1.25); statisticially significant but clinical importance uncertain														
Ixekizumab 80mg Q4W vs placebo	2	RCT	not serious	not serious	serious[a]	not serious	none	1	RCT	not serious	serious[b]	not serious	serious[c]	none
a. different inclusion criteria (bDMARD naive vs. non-responder to 1 or 2 anti TNF alpha); b. only one study available; c. 95% confidence limit crosses MID threshold (1.25); statistically significant but clinical importance uncertain														
Methotrexate 7.5mg/w vs placebo	1	RCT	not serious	serious[a]	not serious	serious[b]	none	no data	no data	no data	no data	no data	no data	no data
a. only one study available; b. 95% confidence limit crosses lines of no effect and MID threshold (1.25); uncertain whether there is any difference														

Sekucinumab 150mg vs. placebo	5	RCT	not serious	not serious	not serious	not serious	none	4	RCT	not serious	not serious	not serious	not serious	none
Secukinumab 150mg+LD vs. placebo	2	RCT	not serious	not serious	not serious	not serious	none	1	RCT	not serious	not serious	serious[a]	not serious	none
	a. Only one study													
Secukinumab 300mg+LD vs. placebo	1	RCT	not serious	not serious	serious[a]	not serious	none	1	RCT	not serious	not serious	serious[a]	not serious	none
	a. Only one study													
Ustekinumab 45mg W0, 4 and Q12W vs placebo	2	RCT	not serious	not serious	not serious	not serious	none	no data	no data	no data	no data	no data	no data	no data
Ustekinumab 90mg W0, 4 and Q12W vs placebo	3	RCT	serious[a]	not serious	not serious	not serious	none	1	RCT	serious[a]	not serious	serious[b]	serious[c]	none
	a. unclear selective outcome reporting 1 of 3 RCTs (RoB = unclear 1/3 and low 2/3); b. only one study; c. 95% confidence interval crosses line of no effect and (0.75), wide confidence interval													

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

ACR 20 reflects on a minimum response of 20% improvement to baseline. Higher improvement percentages will be valued more. ACR is a composite score measuring number of tender and number of swollen joints but also includes patient/physician global assessment as well as pain and functional ability. A stronger focus on patient reported outcomes and quality of life measurements may be valued more by some people.

For safety outcomes see above. In general, direct comparison for safety are hampered by a lack of standardised importance and people may value adverse events and safety profile very differently

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

Indirect evidence for this from above (evidence to decision table for Plaque type psoriasis) can be taken into consideration for this.

Equity

What would be the impact on health equity?

RESEARCH EVIDENCE

- Costs remain barrier to prescribing biologics (11)
- In addition, national regulations and reimbursement situation need to be taken into consideration and treatment algorithms need to be adapted to regional or national specific circumstances.

Acceptability

Is the intervention acceptable to key stakeholders?

RESEARCH EVIDENCE

- Patients are first interested in safety followed by efficacy of treatments, with some variations (10)

- Sociodemographic factors play a role; access and delivery are important attributes
- Costs and drug licencing limit the use of expensive treatment of treatments having a “second line label”.

Recommendations

See main guideline

Justification

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.

For most patients MTX is considered as the first treatment option.(recommendation based on label, long term experience, price, efficacy, safety). .

In case of non-response, TNFs, anti IL12/23 and anti IL17 are considered the alternatives (recommendation based on label, price, efficacy, safety).

Previously, guidelines have given a preference to TNF alpha antagonists over other bDMARDs. In the guideline group's view, a preference for inhibitors of TNF treatments for PsA is no longer mandatory, since the IL-17A antibody treatments might be equally effective, however more data are needed for its real-life long term efficacy, safety and co-medication.

For the selection of a treatment among the anti TNF alpha antagonists and the anti IL17 directed antibodies, no clear hierarchy has been decided upon by the guideline group.

Subgroup considerations

This is already a subgroup, other comorbid conditions are discussed in other chapters.

Implementation considerations

The main barrier to implementation may be the national/local limitation to drug reimbursement, making the prescription of costly treatments difficult.

Monitoring and evaluation

Monitoring and evaluation is to be done on national levels.

- Change in practice performance
- Change in health outcomes
- Change in end-user knowledge and understanding

As an example for national monitoring and evaluation strategies, see BAD (12)or for an example of a cross sectional survey about psoriasis patient care (13)

Research priorities

- -Which treatment is most suitable for specific subtypes of psoriatic arthritis exist (e.g. peripheral, axial, enthesitis, dactylitis)
- How can treatment response be predicted?
- -What is the role of therapeutic drug monitoring?
- -When should a treatment be stopped in case of ceased pain?
- -Which treatments can be combined safely and lead to improved efficacy?

Details of the systematic review update (psoriatic arthritis, results above)

Eligibility criteria

We adhered to the methods as reported in both of the above mentioned reviews. However, we modified the inclusion criteria from Dressler et al. The assessment time of the efficacy outcome modified American College of Rheumatology (ACR) criteria, was not only after 24 weeks but after 12 to 24 weeks since the start of treatment. Hence, studies that were excluded before were also reviewed for inclusion. Studies that were included in both systematic reviews were included in the update.

As safety outcome, we used the proportion of participants with at least one adverse events. We did not take into account guselkumab, bimekizumab and abatacept, because the European Medicines Agency (EMA) has not approved them for the treatment of psoriatic arthritis. We only included randomized controlled trials (RCTs) reporting efficacy outcome and/or safety outcome. The eligibility criteria can be seen in table below.

ELIGIBILITY CRITERIA

Patients	Inclusion: diagnosis of PsA, Pso w/ PsA (at least 80% of the included patient population with PsA where no subgroup analysis was conducted) Adults Exclusion: Other diagnoses e.g. RA Inpatients ≤ 15 patients per study arm at point of randomization
Intervention	Inclusion: DMARDs: methotrexate (MTX), sulfasalazin (SSZ), cyclosporine (CSA) or leflunomide (LEF) Biologics: adalimumab (ADA), etanercept (ETA), golimumab (GOL), infliximab (INF), ustekinumab (UST), secukinumab (SEC), ixekizumab (anti IL17), certolizumab pegol (CZ), including biosimilars for ADA, ETA, GOL and INF Others: apremilast (APR) or tofacitinib (TOF) Exclusion: Guselkumab, bimekizumab and abatacept
Comparator	Inclusion: Comparisons with another included drug and/or placebo Dose comparison studies Exclusion: Comparison with same systematic drug and only different topical drug (in case of patients with primary plaque type psoriasis with sub-analysis for joints)

Outcomes	Inclusion: At least 1 of the following efficacy or safety outcomes at one time point within 12-24 weeks: Efficacy outcomes: 20% improvement in the ACR criteria Safety outcomes: percentage of patients with at least one AE
Study Design	Inclusion: Only RCTs (cross-over, parallel, cluster, factorial) Exclusion: Observational studies Abstracts

Information sources

We searched Medline (via Ovid) using the search strategy from Pham et al (15). The update was run the 25 October 2019. The search contained subject headings and terms for psoriatic arthritis and drugs see end of this section.

Study selection

Duplicates were removed. First, every hit underwent title and abstract screening. Secondly, records underwent full-text screening, both in accordance with the eligibility criteria. Only one reviewer conducted the update.

Data collection and reporting

All records identified were managed with Endnote X8. Data was then extracted using a shorter version of the standardized extraction sheet, as displayed below.

		Study characteristic								Inclusion criteria		Baseline data						Withdrawals			Induction (16-24w): ACR20/50/70					SAE	
First author	Drug	Number (n) randomized	Study duration [w]	Extension	Number of AE withdrawals	Lost to follow-up	discontinuation due to other reasons	Concurrent treatment	Washout phase	Inclusion criteria as defined in the paper	Age	Age mean ±SD/ median (range)	TJC mean ±SD/ median	SJC mean ±SD / median (interquartile range)	HAQ mean±SD / median (interquartile range)	Female n [%]	Weight [kg mean±SD, median(range)]	Number of AE withdrawals	Lost to follow-up	discontinuation due to other reasons	Time of assessment [w]	N	ACR 20 n (%)	ACR 50 n (%)	ACR 70 n (%)	Time of assessment [w]	N (%) of patients with at least one SAE

Methodological quality assessment/ Risk of bias assessment

One reviewer using the Cochrane risk of bias tool assessed the risk of bias of the included studies(16). Each study was evaluated according to the following categories: random sequence generation, allocation concealment, building of participant and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias.

Summary measures

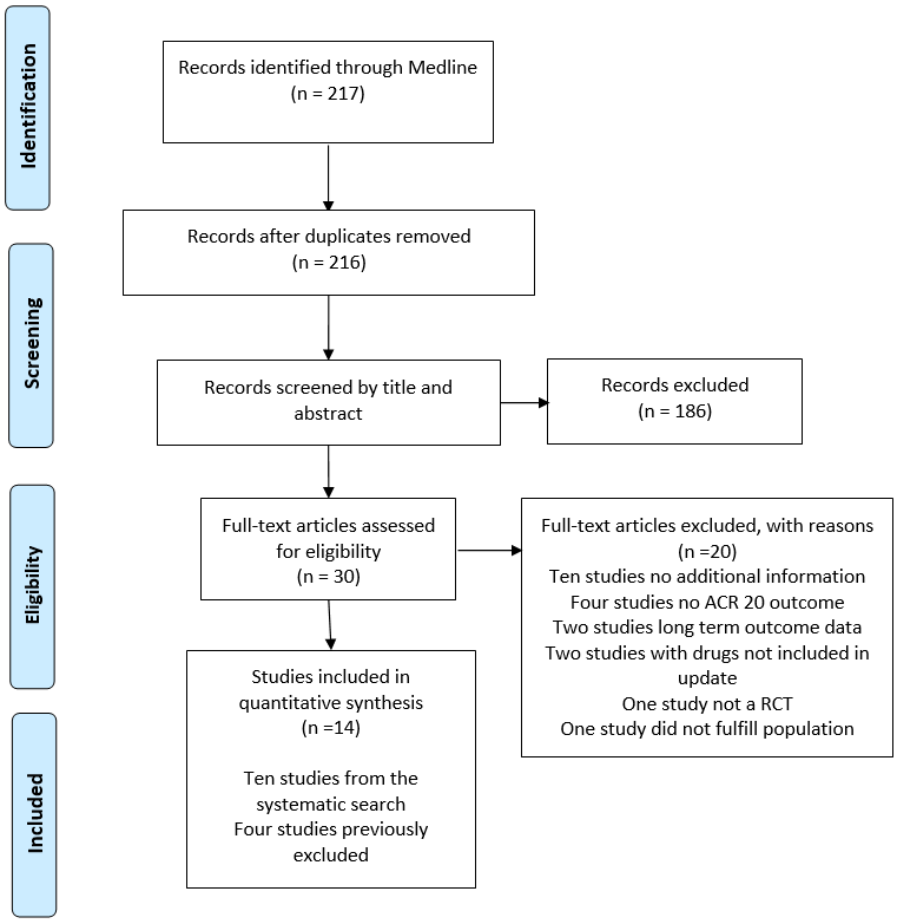
We extracted data from the number of participants as intention to treat(ITT) or modified ITT if available. Review manager 5.3 (RevMan) was used to calculate risk ratios as effect measure for dichotomous outcomes and to estimate 95% confidence intervals. For meta-analyses, data was pooled using random effects model and heterogeneity was assessed with I^2.

Certainty of the evidence

We utilized the GRADE approach (17) to assess the quality of evidence. Gradepro GDT was used to generate summary of findings table and data was imported from RevMan. We evaluated ACR20 and safety outcomes for each treatment comparison.

Results

The search yielded 217 records, 14 new studies were included.



The results of the risk of bias assessment are summarized below:

Title	Overall risk of bias
Genovese 2007 Safety and efficacy of adalimumab in treatment of patients with psoriatic arthritis who had failed disease modifying antirheumatic drug therapy	Unclear RoB
Nash 2018	Unclear RoB

Early and sustained efficacy with apremilast monotherapy in biological-naïve patients with psoriatic arthritis: a phase IIIB, randomised controlled trial (ACTIVE)	
Wells **2018** Apremilast monotherapy in DMARD-naive psoriatic arthritis patients: results of the randomized, placebo-controlled PALACE 4 trial	Unclear RoB
Gladman **2017** Tofacitinib for Psoriatic Arthritis in Patients with an Inadequate Response to TNF Inhibitors. In REVMAN	Low RoB
Mease **2017** Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis	Low RoB
Nash **2018** Efficacy and safety of secukinumab administration by autoinjector in patients with psoriatic arthritis: results from a randomized, placebo-controlled trial (FUTURE 3).	Low RoB
Mease **2018** Secukinumab improves active psoriatic arthritis symptoms and inhibits radiographic progression: primary results from the randomised, double-blind, phase III FUTURE 5 study	Low RoB
Kivitz **2019** Efficacy and Safety of Subcutaneous Secukinumab 150 mg with or Without Loading Regimen in Psoriatic Arthritis: Results from the FUTURE 4 Study	Low RoB
Kavaugh **2017** Safety and Efficacy of Intravenous Golimumab in Patients With Active Psoriatic Arthritis: Results Through Week Twenty-Four of the GO-VIBRANT Study .	Low RoB
Gottlieb **2009** Ustekinumab, a human interleukin 12/23 monoclonaREVMAN, Study included Outcome at 12 week, NCT00267956l antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial.[Erratum appears in Lancet. 2009 Apr 18;373(9672):1340], [Erratum appears in Lancet. 2010 Nov 6;376(9752):1542]	Low RoB
Mease **2019** A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naive patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial	High RoB
Mease **2000** Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial	High RoB
Mease **2019** Etanercept and Methotrexate as Monotherapy or in Combination for Psoriatic Arthritis: Primary Results From a Randomized, Controlled Phase III Trial (SEAM-PsA)	Low RoB
Van Mense **2019**	High RoB

Achieving remission in psoriatic arthritis by early initiation of TNF inhibition: a double-blind, randomised, placebo-controlled trial of golimumab plus methotrexate versus placebo plus methotrexate	

A summary of the results of the meta-analysis and the GRADE evaluation are shown below, all details are available upon request from euroguiderm@debm.de.

Included here were all treatments that are licensed for psoriatic arthritis to be congruent with the previous review. However, the guideline chapter only includes those that are licensed for psoriasis.

A brief overview of the newly included studies is also included below.

	Patients achieving ARC20			Patients with at least one		
Placebo comparisons						
	RR	95% CI	Quality of the Evidence (GRADE)	RR	95% CI	Quality of the Evidence (GRADE)
SEC 150mg vs. PBO	2.44	2.10 to 2.84	HIGH	1.03	0.95 to 1.12	HIGH
SEC 150mg + LD vs. PBO	2.06	1.70 to 2.49	HIGH	1.01	0.89 to 1.15	MODERATE
TOF 10mg BID vs. PBO	1.89	1.49 to 2.39	HIGH	1.23	1.00 to 1.50	MODERATE
UST 45mg vs PBO	1.95	1.52 to 2.50	HIGH	n.d.		
APR 30mg BID vs. PBO	1.94	1.59 to 2.38	MODERATE	1.24	1.12 to 1.36	LOW
ADA 40mg EOW vs. PBO	3.35	2.24 to 4.99	MODERATE	0.67	0.50 to 0.89	VERY LOW
APR 20mg BID vs PBO	1.86	1.49 to 2.31	MODERATE	1.27	1.15 to1.41	LOW
CZP 400mg vs. PBO	2.36	1.68 to 3.31	MODERATE	1.05	0.90 to 1.23	MODERATE
CZP 200mg vs. PBO	2.71	1.95 to 3.76	MODERATE	1.01	0.86 to 1.19	MODERATE
GOL 50mg vs. PBO	4.20	2.51 to 7.03	MODERATE	1.14	0.95 to 1.38	LOW
GOL 100mg vs. PBO	4.92	2.96 to 8.17	MODERATE	1.10	0.90 to 1.33	LOW
GOL 2mg/kg vs. PBO	3.45	2.69 to 4.44	MODERATE	1.14	0.93 to 1.40	LOW
INF 5mg/kg vs. PBO	4.38	2.24 to 8.56	MODERATE	1.13	0.87 to 1.47	LOW
IXE 80mg Q2W vs. PBO	2.21	1.71 to 2.86	MODERATE	1.39	1.09 to 1.78	LOW
IXE 80mg Q4W vs. PBO	2.25	1.59 to 3.18	MODERATE	1.41	1.10 to 1.79	LOW
SEC 300mg + LD vs. PBO	2.28	1.87 to 2.80	MODERATE	1.02	0.89 to 1.16	MODERATE
TOF 5mg BID vs. PBO	1.77	1.29 to 2.44	MODERATE	1.20	0.98 to 1.47	MODERATE
UST 90mg vs PBO	2.26	1.80 to 2.82	MODERATE	0.96	0.75 to1.24	VERY LOW
ETA 25mg BIW vs. PBO	4.05	2.56 to 6.40	LOW	n.d.		
LEF 100mg vs. PBO	1.70	0.99 to 2.92	LOW	1.12	0.97 to 1.29	LOW
MTX 7.5mg vs. PBO	1.82	0.97 to 3.40	LOW	n.d.		
SSZ 0.2mg QD vs. PBO	1.29	0.90 to 1.86	VERY LOW	1.29	0.90 to 1.86	VERY LOW
Head-to-head comparisons:						
ETA 50mg + MTX vs. MTX 20mg QW	1.28	1.11 to 1.48	LOW	1.01	0.92 to 1.11	MODERATE
LEF 100mg vs. MTX 10mg	1.01	0.84 to 1.21	LOW	n.d.		
TOF 5 mg BID vs ADA 40mg Q2W	0.97	0.75 to 1.26	LOW	0.85	0.62 to 1.16	LOW
GOL 50mg + MTX vs. MTX 25 mg QW	1.45	1.00 to 2.11	VERY LOW	0.88	0.70 to 1.10	VERY LOW
INF 5mg/kg + MTX vs. MTX 15mg/kg	1.40	1.07 to 1.84	VERY LOW	1.65	1.08 to 2.52	VERY LOW
IXE 80mg Q2W vs. ADA 40mg Q2W	1.08	0.86 to 1.36	VERY LOW	1.02	0.83 to 1.25	MODERATE
IXE 80mg Q4W vs. ADA 40mg Q2W	0.96	0.86 to 1.06	VERY LOW	1.14	1.01 to 1.28	VERY LOW
LEF 100mg vs. MTX 10mg	1.01	0.84 to 1.21	LOW	n.d.		

The results are summarized below. Full data extraction tables of the studies including during this update are available upon request from euroguiderm@debm.de

First author	Drug	Number (n) randomized	Time of assessment [w]	N	ACR20 n(%)	ACR50 n(%)	ACR70 n(%)	Time of assessment [w]	N / % of patients with at least 1 AE	Time of assessment [w]	N (%) of patients with at least one SAE
ADA											
Genovese 2007	ADA 40mg (in 0.8ml syring) s.c. EOW for 12wks	51	12	51	20 39.2%	13 25.5%	7 13.8%	12	27/51 52.9%	12	1/51 2.0%
	PBO (in 0.8ml sying) s.c. EOW for 12 wks	51 (ITT 49)		51 (ITT 49)	8 16.3%	1 2.0%	0%		39/49 79.6%		2/49 4.1
ETA											
Mease 2000	ETN 25mg SC (twice weekly)	30	12	30	22 73.73%	15 50.0%	4 13%	12	nr	12	0/30
	PBO SC (twice weekly)	30 (26 completed study last obs carried forward)		30	4 13.3%	1 3.3%	0		nr		1/30
Mease 2019 **SEAM-PsA** **NCT02376790**	MTX 2.5mg p.o (starting 10mg/week up to 20mg/week) + SC PBO weekly	284	24	284	144/284 50.7%	77/252 30.6%	35/253 13.8%	24	nr	24	nr
	ETN 50mg SC (weekly)	284		284	173/284 60.9%	114/257 44.4%	75/257 29.2%		nr		nr
	ETN 50mg SC (weekly) + MTX p.o (target dose 20mg/wk)	283		283	184/283 65.0%	117/256 45.7%	71/256 27.7%		nr		nr
GOL											
Kavanaugh 2017 **GO Vibrant** **NCT02181673**	GOL i.v 2 mg/kg at weeks 0 and 4 and every 8 weeks	241 (240 received GOL)	14	241	181 75.1%	105 43.6%	59 43.6%	24	111/240 46.3%	24	7/240 2.9%
	PBO i.v at weeks 0 and 4 and every 8 weeks	239		239	52 21.8%	15 6.3%	15 6.3%		97/239 40.6%		8/239 3.3%
van Mens 2019 **NCT01871649**	GOL 50 mg monthly + MTX 15mg weekly up to 25 mg weekly	26	22	26	Circa 22 85%	circa 21 81%	Circa 15 58%	22	21/26 80.8%	22	0/26
	MTX 15mg weekly up to 25 mg weekly + PBO	25 (ITT 24)		24	Crica 14 58%	Circa 8 33%	Circa 3 13%		22/24 91.6%		1/24 0,04

First author	Drug	Number (n) randomized	Time of assessment [w]	N	ACR20 n(%)	ACR50 n(%)	ACR70 n(%)	Time of assessment [w]	N / % of patients with at least 1 AE	Time of assessment [w]	N (%) of patients with at least one SAE
APR											
Nash 2018	APR 30mg BID for 52 weeks	110		110	42 38.2%				73/109 67.0%		3/109 2.8%
ACTIVE **NCT01925768**	PBO for 16w, w16 non-responders EE & re-randomized APR 30mg BID if pts had <10% improvement in SJC & TJC, all other at w24	109	16	109	22 20.2%			24	69/109 63.3%	24	5/109 4.6%
Wells 2018	APR 20 mg tablets p.o. BID	175		175	49 28%	20 11,45%	7 4.0%		87/175 49.7%		3/175 1.7%
	APR 30mg tablets p.o. BID	176		176	54 30.7%	20 11.4%	7 4.0%		99/175 56.6%		1/175 0.6%
PALACE 4 **NCT01307423**	PBO tablets BIP p.o., EE if pts ≤ 20% improvement in SJC and TJC at wk 16, at w24 remaining PBO pts were re-randomised to APR20mg or APR30Mg BIP	176	16	176	28 15.9%	8 4.5%	2 1.1%	24	73/176 41.5%	24	5/176 2.8%
TOF											
Gladmann 2017	tofacitinib 5 mg BID	131	12 week (study has also 24 weeks but placebo has a crossover to treatment)	131	65 49,6%	39 29,8%	22 16,8%		72/131 55%		1/131 1%
OPAL Beyond **NCT01882439**	tofacitinib 10 mg BID	132		132	62 47,0%	37 28,0%	19 14,4%	12	70/132 53%	12	3/132 2%
	PBO, advanced to TOF 5mg or 10mg in blinded manner at 3M	131		131	31 23,7%	19 14,5%	13 9,9%		58/131 44%		3/132 2%
Mease 2017 **OPAL BROADEN** **NCT0187766**	TOF 5mg BID	107	12 weeks	107	54 50.5%	30 28.0%	18 16.8%	12 weeks	42/107 39.3%	12 weeks	3/107 2.8%
	TOF 10mg BID	104		104	63 60.6%	42 40.4%	15 14.4%		47/104 45.2%		1/104 1.0%
	ADA 40mg sc Q2W	106		106	55 51.9%	35 33.0%	20 18.9%		49/106 46.2%		1/106 0.9%
	PBO	105		105	35 33.3%	10 09.5%	5 4.8%		37/105 35.2%		1/105 1.0%

First author	Drug	Number (n) randomized	Time of assessment [w]	N	ACR20 n(%)	ACR50 n(%)	ACR70 n(%)	Time of assessment [w]	N / % of patients with at least 1 AE	Time of assessment [w]	N (%) of patients with at least one SAE
SEC											
Nash 2018	SEC 300mg SC QW w0,1,2,3,4 then every 4w	139		139	67 48.2%	48 34.5%			76/139 54.7%		3/139 2.2%
FUTURE 3	SEC 150mg SC QW w0,1,2,3,4 then every 4w	138	24	138	58 42.0%	26 18.8%		16	80/138 58.0%	16	5/138 3.6%
NCT01989468	PBO w0,1,2,4 then every 4w	137		137	22 16.1%	12 8.8.%			77/137 56.2%		9/137 6.6%
Kivitz 2019	Sec 150mg QW with loading of 150mg, w0,1,2,3,4 then every 4w	114		114	47 41.2%	26 22.8%	9 /.9%				
FUTURE 4	SEC 150mg QW without loading, w0,1,2,3,4 then every 4w	113	16	113	45 39.8%	19 16.8%	10 8.8%			104	
(NCT02294227	PBO QW, w0,1,2,3,4 then every 4w	114		114	21 18.4%	7 6.1%	1 0.9%				
Mease 2018	SEC 300mg QW with LD, w0,1,2,3,4 then every 4w	222		222	139 62.6%	39.6%	20.3%		140/222 63.1%		7/222 3.2%
FUTURE 5	SEC 150mg QW with LD w0,1,2,3,4 then every 4w	220		220	122 55.5%	35.9%	18.2%		138/220 62.7%		9/220 4.1%
NCT02404350	SEC 150mg QW without LD w0,1,2,3,4 then every 4w	222	16	222	132 59.5%	32.0%	14.9%	24	136/222 61.3%	24	6/222 2.7%
	PBO w0,1,2,3,4 then every 4w	332		332	91 27.4%	8.1%	4.2%		206/332 62.0%		12/332 3.6%
IXE											
Mease 2019	IXE 80mg SC every Q4W with160 mg LD in w0, or Q2W if moderate to severe psoriasis	283		283	195 68.9%	143 50.5%	90 31.8%		197/283 69.6%		10/283 3.5%
SPIRIT H2H			24					24		24	
Open label study	ADA 40mg SC Q2W or 80mg LD then 40mg Q2W if moderate to severe psoriasis	283		283	204 72.1%	132 46.6%	73 25.8%		173/283 61.1%		24/283 8.5%
NCT03151551											
UST											
Gottlieb 2009 Kavanaugh 2010	UST 90mg sc. Q1wk at wk 0,1,2,3; crossover to placebo at wk 12+16	76	12	76 (ITT, 74 completed week 12)	32 42%	19 25%	5 7%	12	46/76 60.5%	12	0 0%
NCT00267956	PBO sc. Q1wk at wk 0,1,2,3, UST 90mg at wk 12+ 16	70		70 (ITT, 63 completed week 12)	10 14%	8 11%	0 0%		44/70 62.9%		3/70 4.2%

Search strategy for the review on psoriasis arthritis: MEDLINE OVID; from Pham et al 2019]

#	Searches		
1	exp Arthritis, Psoriatic/	32	30 and 31
2	(Psoria* adj3 arthr*).ab,ti.	33	Randomized Controlled Trials as Topic/
3	exp Antibodies, Monoclonal/	34	randomized controlled trial/
4	exp Adalimumab/	35	Random Allocation/
5	adalimumab.ab,ti.	36	Double Blind Method/
6	exp Certolizumab Pegol/	37	Single Blind Method/
7	certolizumab pegol.ab,ti.	38	clinical trial/
8	exp Ustekinumab/	39	clinical trial, phase i.pt.
9	ustekinumab.ab,ti.	40	clinical trial, phase ii.pt.
10	exp Infliximab/	41	clinical trial, phase iii.pt.
11	infliximab.ab,ti.	42	clinical trial, phase iv.pt.
12	exp Etanercept/	43	controlled clinical trial.pt.
13	etanercept.ab,ti.	44	randomized controlled trial.pt.
14	golimumab.ab,ti.	45	multicenter study.pt.
15	secukinumab.ab,ti.	46	clinical trial.pt.
16	guselkumab.ab,ti.	47	exp Clinical Trials as topic/
17	ixekizumab.ab,ti.	48	or/33-47
18	apremilast.ab,ti.	49	(clinical adj trial$).tw.
19	tofacitinib.ab,ti.	50	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.
20	biologic*.ab,ti.	51	PLACEBOS/
21	(DMARD* or diseas* modif* anti?rheuma* drug* or (anti?rheuma* adj2 drug*) or (anti?rheuma* adj2 agent*) or (monoclonal adj2 antibod*)).ab,ti.	52	placebo$.tw.
22	exp Antirheumatic Agents/	53	randomly allocated.tw.
23	exp Methotrexate/	54	(allocated adj2 random$).tw.
24	(MTX* or methotrexat*).ab,ti.	55	or/49-54
25	exp Sulfasalazine/	56	48 or 55
26	(sulfazalazin* or sulphasalazin* or sulphazalazin* or sulfasalazin* or SSZ*).ab,ti.	57	case report.tw.
27	exp Cyclosporine/	58	letter/
28	(cyclosporin* or ciclosporin* or csa*).ab,ti.	59	historical article/
29	(leflunomid* or lef*).ab,ti.	60	or/57-59
30	1 or 2	61	56 not 60
31	3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	62	32 and 61

Excluded full-texts with reasons:

Author	Year	Title	Reason for exclusion
I. B. McInnes, et al.	2017	Secukinumab sustains improvement in signs and symptoms of psoriatic arthritis: 2 year results from the phase 3 FUTURE 2 study	(no additional information, same study)
D. van der Heijde, et al.	2018	4-year results from the RAPID-PsA phase 3 randomised placebo-controlled trial of certolizumab pegol in psoriatic arthritis	(no additional information)

D. van der Heijde, et al.	2018	Efficacy and Safety of Ixekizumab in Patients with Active Psoriatic Arthritis: 52-week Results from a Phase III Study (SPIRIT-P1)	(no additional information)
J. A. Walsh, et al.	2018	Efficacy of certolizumab pegol with and without concomitant use of disease-modifying anti-rheumatic drugs over 4 years in psoriatic arthritis patients: results from the RAPID-PsA randomized controlled trial	(long term data study already included by dressler)
L. C. Coates, et al.	2018	Secukinumab provides sustained PASDAS-defined remission in psoriatic arthritis and improves health-related quality of life in patients achieving remission: 2-year results from the phase III FUTURE 2 study	(no additional information)
S. Cohen, et al.	2019	Decreased Injection Site Pain Associated with Phosphate-Free Etanercept Formulation in Rheumatoid Arthritis or Psoriatic Arthritis Patients: A Randomized Controlled Trial	(no ACR20 outcome)
S. Dauth, et al.	2018	[Value of combining biologics with methotrexate for treatment of psoriatic arthritis-questions remain]	(no RCT)
H. M. Y. de Jong, et al.	2019	Sustained remission with methotrexate monotherapy after 22-week induction treatment with TNF-alpha inhibitor and methotrexate in early psoriatic arthritis: an open-label extension of a randomized placebo-controlled trial	(no ACR20 outcome)
A. Deodhar, et al.	2018	Efficacy and safety of guselkumab in patients with active psoriatic arthritis: a randomised, double-blind, placebo-controlled, phase 2 study	(not approved by EMA for PsA)
M. C. Genovese, et al.	2018	Safety and efficacy of ixekizumab in patients with PsA and previous inadequate response to TNF inhibitors: week 52 results from SPIRIT-P2	(no additional information)
S. Glatt, et al.	2018	Dual IL-17A and IL-17F neutralisation by bimekizumab in psoriatic arthritis: evidence from preclinical experiments and a randomised placebo-controlled clinical trial that IL-17F contributes to human chronic tissue inflammation	(not approved by EMA for PsA)
A. B. Gottlieb, et al.	2018	Ixekizumab improves patient-reported outcomes up to 52 weeks in bDMARD-naive patients with active psoriatic arthritis (SPIRIT-P1)	(no additional info)
M. Haroon, et al.	2018	Inflammatory back pain in psoriatic arthritis is significantly more responsive to corticosteroids compared to back pain in ankylosing spondylitis: a prospective, open-labelled, controlled pilot study	(no ACR20 outcome, pilot study)
A. Kavanaugh, et al.	2019	Radiographic Progression Inhibition with Intravenous Golimumab in Psoriatic Arthritis: Week 24 Results of a Phase III, Randomized, Double-blind, Placebo-controlled Trial	(no additional info)
A. Kavanaugh, et al.	2019	Ixekizumab improves patient-reported outcomes in patients with active psoriatic arthritis and inadequate response to tumour necrosis factor inhibitors: SPIRIT-P2 results to 52 weeks	(no additional info SPIRIT p2)

I. B. McInnes, et al.	2018	Secukinumab provides rapid and sustained pain relief in psoriatic arthritis over 2 years: results from the FUTURE 2 study	(no additional info)
M. Ohtsuki, et al.	2019	Efficacy and safety of risankizumab in Japanese patients with moderate to severe plaque psoriasis: Results from the SustaIMM phase 2/3 trial	(Fewer than 20% of patients in any treatment group had psoriatic arthritis)
V. Strand, et al.	2019	Effect of tofacitinib on patient-reported outcomes in patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors in the phase III, randomised controlled trial: OPAL Beyond	(a same trial opal beyond data in ANN no outcome of interest)
V. Strand, et al.	2019	Tofacitinib or adalimumab versus placebo: patient-reported outcomes from OPAL Broaden-a phase III study of active psoriatic arthritis in patients with an inadequate response to conventional synthetic disease-modifying antirheumatic drugs	(no additional info same trial OPAL Broaden ANN)
D. van der Heijde, et al.	2019	Secukinumab provides sustained low rates of radiographic progression in psoriatic arthritis: 52-week results from a phase 3 study, FUTURE 5	(long term outcomes)

Appendix 5 Diabetes Mellitus

Diabetes mellitus: Systematic review of the evidence on psoriasis treatment and diabetes mellitus

We conducted a "Systematic review of the efficacy, effectiveness and safety of topical and systemic treatments for psoriasis in patients with diabetes mellitus", for which a protocol was published on PROSPERO (CRD42018087908). The work was conducted as part of a doctoral thesis by Rhea Jakubzyk, who gave permission to print her work here. Passenges here may be identical to her thesis.

For the guideline, the recommendations focus on the systemic treatment options licensed for plaque type psoriasis.

Eligibility criteria

We included all studies on adult patients with a clinical diagnosis of psoriasis and a concomitant diabetes mellitus of any type being treated for psoriasis.

The interventions were specified to be topical treatment (urea, salicylic acid, calcineurin-inhibitors (pimecrolimus, tacrolimus), dithranol, corticosteroids (betamethasone, mometasonfuroat), tazaroten, coal tar, vitamin D3 derivate (calcipotriol, tacalcitol, calcitriol, calcipotriol and betamethasone) or systemic treatment (aciretin, ciclosporin, fumarates, methotrexate, apremilast) for psoriasis including biologicals (Anti TNF-alpha: etanercept, infliximab, adalimumab; anti-IL12/23: ustekinumab; Anti-IL17: secukinumab, ixekizumab, brodalumab; Anti-IL23). We included studies comparing the intervention to placebo or another treatment and those without comparator.

The following outcomes were of interest:

- Change in skin lesions based on PASI (Psoriasis Area Severity Index) or PGA (Physician Global Assessment) or another study specific assessment.
- Fasting plasma glucose, HbA1c or insulin sensitivity measured by HOMA (Homeostasis Modell Assessment) or other study specific outcomes
- Type and proportion of other adverse events
- Quality of life based on SF-36 (The Short Form (36) Health Survey), DLQI (Dermatology Life Quality Index) or another study specific assessment.

Wherever possible, we evaluated the outcomes at different timings, based on what was reported in the publications (e.g. short-term, long-term).

Included were randomized controlled trials, clinical trials (with and without comparison group), cohort studies, case control studies and cross sectional studies. We used a step-wise approach for including studies (for each study drug and comparator) following the hierarchy of evidence (Murad et al., 2016).

We excluded studies on patients with psoriatic arthritis only because of the different pathophysiology and treatment options. We also excluded studies with less than 100 patients to minimize bias.

Information sources

Three databases were searched systematically (MEDLINE Ovid from 1946, Embase Ovid from 1974 and The Cochrane Central Register of Controlled Trials (CENTRAL); updated last in September 2019. Furthermore, we examined the reference lists of included studies to identify references to relevant trials. The full search strategy is shown below.

Study selection

We screened all identified abstracts/titles for eligibility. Included title/abstracts were then screened as full texts based on the above listed eligibility criteria.

Data collection and reporting

Endnote was used to manage all records. One reviewer performed the screening and did the data extraction using a standardized form. A second reviewer checked the screening. We recorded all full-texts excluded and the primary reason for exclusion (see below).

The following items were extracted: Author, year of publication, country in which the study took place, study design, inclusion and exclusion criteria, baseline characteristics of the included patients, details of the interventions, details of any co-interventions, number and reasons for drop-out, type of adverse events and proportion of patients experiencing adverse events and serious adverse events, proportion of patients who experienced worsening of diabetes parameters, proportion of patients who showed an improvement in skin lesions, proportion of patients who showed an improvement in quality of life, time of assessment of endpoints and number/rate of patients assessed.

Methodological quality assessment/ Risk of bias assessment

We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations (OCEBM Levels of Evidence Working Group and * OCEBM Levels of Evidence Working Group = Jeremy Howick, 2011). We assigned Levels of Evidence for all studies using the Center of Evidence Based Medicine Oxford recommendations (OCEBM Levels of Evidence Working Group and * OCEBM Levels of Evidence Working Group = Jeremy Howick, 2011). To assess risk of bias in randomized trials we additionally used the RoB 2.0 tool (Higgins JPT, 2016). We planned to use the ROBINS-I tool for controlled non-randomized studies of interventions but none of these type were included (Sterne et al., 2016).

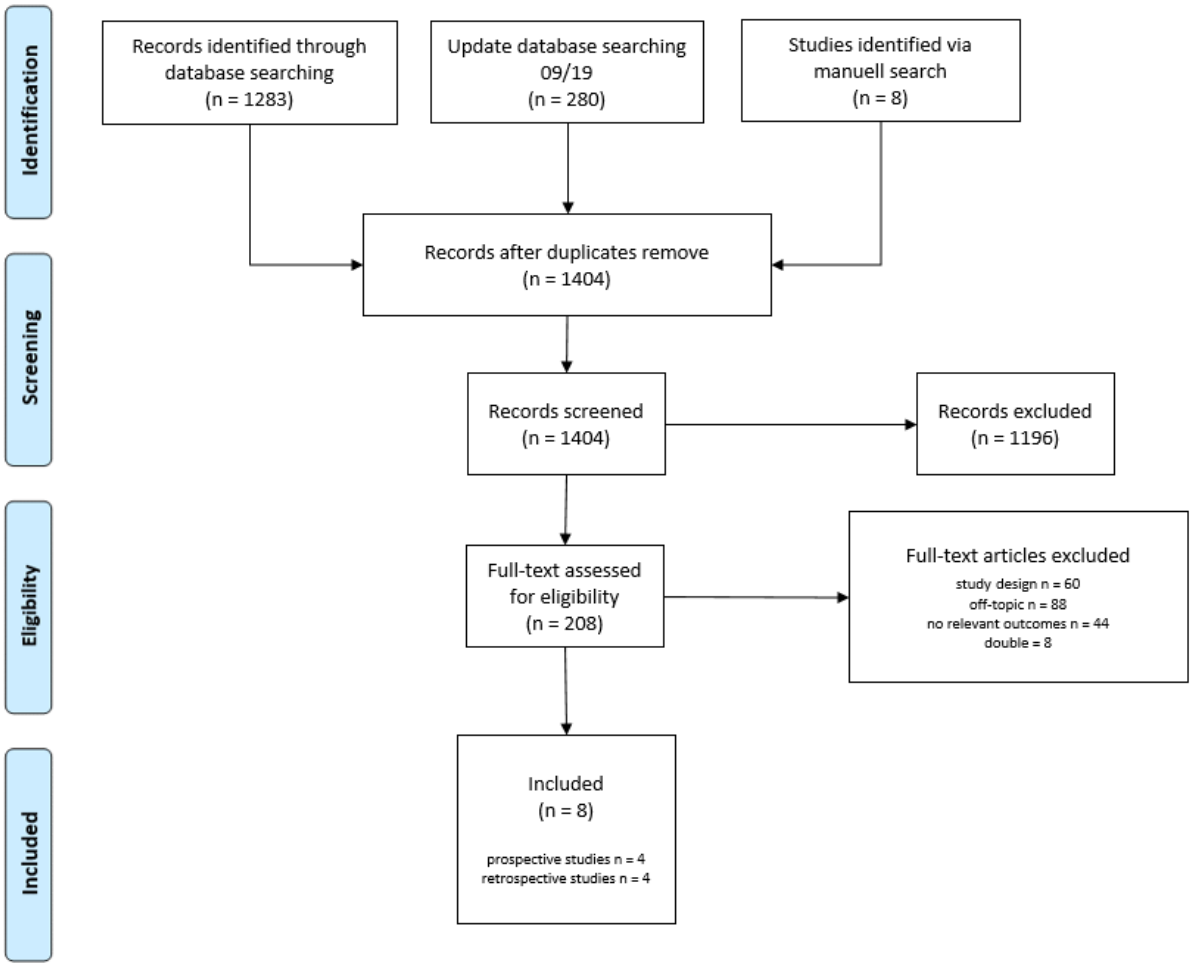
Summary measures

Data was summarized and sorted by study type (see Table 2 and 3).

Results

Our search yielded 1404 citations, eight of which fulfilled the inclusion criteria (September 2019; see study selection flow chart). Four prospective studies (Pinter et al., 2019, Al-Mutairi and Shabaan, 2016, Koenig et al., 2011, Kimball et al., 2011), one study based on registry data (Kalb et al., 2015) and three retrospective studies (Hong et al., 2019, Wu et al., 2014, Wu et al., 2015) were included.

We did not find any studies on aciretin, apremilast, brodalumab, fumarates, guselkumab, ixekizumab, risankizumab, tildrakizumab that reported diabetes mellitus outcomes.



Based on the "Levels of Evidence - Center of Evidence Based Medicine Oxford recommendations" four prospective studies were categorized level 2 (18-21) and four retrospective studies level 3 (22-26). Results of the additional assessment for prospective randomized studies are shown in Table 1 (18-21, 27-31).

Author (Year)	Original study	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Al-Mutairi, N., Shabaan, D. (2016)		⊕	⊖	⊕	⊖	?	⊕
Kimball, A. B. et al. (2011)	Menter, A. et al. (2008)	⊖	⊖	⊖	⊖	⊖	⊖
Koenig, A. S. et al. (2011)	Strobal, R. et al. (2013)	?	⊕	⊖	⊖	⊖	?
Pinter, A. et al. (2019)	Blauvelt, A. et al. (2017)	⊖	⊖	⊖	⊖	⊖	⊖
	Langley, R.G. e al. (2014)	?	?	⊖	?	⊖	?

Abbreviation: ⊕ = high risk of bias ? = some concerns ⊖ = low risk of bias

TABLE 1 RISK OF BIAS IN PROSPECTIVE STUDIES

Data for overall 3503 patients with psoriasis and diabetes mellitus was extracted. Summarized results, sorted by study type are shown below.

Prospective studies

Title	Author (Y)	Original study	Intervention	Duration of treatment (M)	Patients (n)	Patients with diabetes (n)	Follow-up (M)	Age (Y) (Ø±SD)	♀ (%)	Psoriasis-score at baseline (Ø±SD)	Quality of life at baseline (Ø±SD)	Diabetes parameters at baseline (Ø±SD)	Outcomes: End of follow-up (M)	Outcomes: Psorias-score e.g. PASI 75	Outcomes: Mean change of quality of life (Ø±SD)	Outcomes: Mean change of diabetes parameters (Ø±SD)	Outcomes: Adverse events
Efficacy and safety of adalimumab among patients with moderate to severe psoriasis with co-morbidities: Subanalysis of results from a randomized, double-blind, placebo-controlled, phase III trial	Kimball, A. B. et al. (2011)	Menter, A. et al. (2008)	ADA (80mg/40mg)	4	814	73	13	47.2±12.4[1]	35%[1]	PASI 19.3±7.2	/	/	4	PASI75 n=46 (63%)	DLQI -7.1±6.3	Glucose (mmol/L) -0.47	SAE not infectios n=2 (2.7%) SAE infectios n= 1 (1.4%) Dropout because of AE n=1 (1.4%)
			Placebo		398	52		48.8±12.6[1]	36%[1]	PASI 19.1±7.6				PASI75 n=2 (3.8%)	DLQI -1.3±5.8	Glucose (mmol/L) -0.65	SAE not infectios n=2 (3.8%) SAE infectios n=0 (0%) Dropout because of AE n=2 (3.8%)
Characterization of responder groups to secukinumab treatment in moderate to severe plaque psoriasis	Pinter, A. et al. (2019)	Blauvelt, A. et al. (2017) Langley, R.G. et al. (2014)	SEC (300mg)	4	867	69	4	44.8[1]	/		/		4	PASI100 n=6.6/69 (9.6%) PASI75 n=50/69 (72.5%) PASI50 n=9.4/69 (13.6%) <PASI50 n=3/69 (4.3%)	/	/	/
			UST (45/90mg)		318	97.5		44.8[1]						PASI100 n=23.5/97.5 (24.1%) PASI75 n=57/97.5 (58.5%) PASI50 n=9/97.5 (9.2%) <PASI50 n=8/97.5 (8.2%)			
			ETA (50mg)		298	27		43.6[1]						PASI100 n=1/27 (3.7%) PASI75 n=15/27 (55.6%) PASI50 n=8/27 (29.6%) <PASI50 n=3/27 (11.1%)			
Impact of etanercept therapy on glycemic control in a cohort of psoriatic patients: The pristine trial	Koenig, A.S. et al. (2011)	Strobal, R. et al. (2013)	ETA (50mg/100mg)	3	273	35	3	44[1]	30[1]	21[1]	/	HbA1c (%) 7.0 FPG (mmol/l) 6.8 IS 5.3 PI (mcU/mL) 14.0	3	/	/	HbA1c (%) -0.3 FPG (mmol/l) 0.1 IS 1.1 PI (mcU/mL) 3.0	/
Effects of tumor necrosis factor alpha inhibitors extend beyond psoriasis: insulin sensitivity in psoriasis patients with type 2 diabetes mellitus	Al-Mutairi, N., Shabaan, D. (2016)		ADA (n=14) ETA (n=8) IFX (n=12)	6	34 (35 randomised)	34 (35 randomised)	6	43.7±21.6	52.9% (18/34)	/	/	HbA1c (%) 8.4±0.38 FPG (mmol/L) 10±25 IS 5.9±0.52	6	/	/	HbA1c (%) -1.3 FPG (mmol/L) -2.74±0.34 IS 1.2±0.4	/
			Topic cortikosteroids, calcipotriol (n=8) CsA (n=7) MTX (n=14)		29 (35 randomised)	29 (35 randomised)		47.7±14.2	51.7% (15/29)			HbA1c (%) 8.1±0.21 FPG (mmol/L) 11±0.4 IS 5.4±0.31				HbA1c (%) 0.2 FPG (mmol/L) -0.02±0.16 IS -0.3±0.12	

	Title	Author (Y)	Intervention	Duration of treatment (M)	Patients (n)	Patients with diabetes (n)	Age (Y) (Ø±SD)	♀ (%)	Psoriasis-score at baseline (Ø±SD)	Quality of life at baseline (Ø±SD)	Diabetes parameters at baseline (Ø±SD)	Outcomes: End of follow-up (M)	Outcomes: Psorias-score e.g. PASI 75	Outcomes: Mean change of quality of life (Ø±SD)	Outcomes: Mean change of diabetes parameters (Ø±SD)	Outcomes: Adverse events
Registry data	Risk of Serious Infection With Biologic and Systemic Treatment of Psoriasis: Results From the Psoriasis Longitudinal Assessment and Registry (PSOLAR)	Kalb, R. E. et al. (2015)	ADA (n=331) ETA (n=221) IFX (n=161) UST (n=440)	21[1]	11461	1459 (12.7%[1])	48.5±13.8[1]	44.9%[1]	/	/	/	/	/	/	/	"presence of diabetes mellitus was found to be a significant predictor of serious infection" (HR, 1.7; 95% CI, 1.25-2.23; p < 0.001)
			Non-MTX/Non-biologics (n=204)													/
	Risk factors for increased serum creatinine level in patients with psoriasis treated with cyclosporine in a real-world practice	Hong, J. R. et al. (2019)	CsA	3	398	37 (9.3%)	45.3±15.6[1]	44.2%[1] (176/398)	PASI 11.5[1]	/	/	/	/	/	/	"relative risk of a greater than 10% increase in serum creatinine levels was increased in diabetic patients" (HR 2.34; 95% CI, 1.59–3.45; p <0 .001)
Retrospective studies	No association between TNF inhibitor and methotrexate therapy versus methotrexate in changes in hemoglobin A1C and fasting glucose among psoriasis, psoriatic arthritis, and rheumatoid arthritis patients	Wu, J. J. et al. (2015)	MTX + TNFi (ADA, ETA,IFX)/GOL	12	118	99 (83.9%[2])	59.4±9.43[2]	70.3%[2] (83/118)	/	/	HbA1c (%) 6.9±1.7	1-12	/	/	HbA1c (%) -0.1±1.0	/
					121	34 (28.1%[2])	57.7±9.78[2]	73.9%[2] (86/121)			FPG (mg/dl) 102.5±22.1				FPG (mg/dl) 3.7±18.6	
			MTX		344	247 (71.8%[2])	64.7±10.36[2]	67.2%[2] (231/344)	/	/	HbA1c (%) 6.7±1.2				HbA1c (%) 0.0±0.8	
					524	92 (17.6%[2])	64.7±11.16[2]	73.9%[2] (387/524)			FPG (mg/dl) 104.1±28.1				FPG (mg/dl) 1.3±24.5	
	Initiation of TNF inhibitor therapy and change in physiologic measures in psoriasis	Wu, J. J. et al. (2014)	TNFi	12	1274	209/1274 (16.4%[2])	46.7±13.8[2]	48.5%[2] (618/1274)	/	/	/	6	/	/	FPG (mg/dl; n=35 diabetes patients) 1.5±40.7	/
			MTX		979	163/979 (16.7%[2])	50.9±14.4[2]	52.3%[2] (512/979)							FPG (mg/dl; n=43 diabetes patients) -15.6±54	
			Phototherapy		4309	711/4309 (16.5%[2])	52±15.9[2]	47.1%[2] (2029/4309)							/	

Abbreviation:
ADA = Adalimumab; AE = Adverse Event; CsA = Cyclosporine A; DLQI = Dermatology Life Quality Index; ETA = Etanercept; FPG = Fasting Plasma Glucose; GOL = Golimumab; HbA1c = Haemoglobin A1c; IFX = Infliximab; IS = Insuline Sesitivity measured by HOMA (Homeostasis Modell Assessment); M = Month; MTX = Methotrexate; Ø±SD = Mean ±standard deviation; PASI = Psoriasis Area Severity Index; PASI100/75/50 = 100%/75%/50% improvement in PASI; PI = Plasma Insuline; SAE = Severe Adverse Event; SEC = Secukinumab; TNFi = Tumor Necrosis Factor Inhibitor; UST = Ustekinumab; Y = Year

Search strategy for the review on psoriasis and diabetes mellitus (Embase via Ovid)

1. exp Psoriasis/ or Psoria*.mp.	34. narrow band uvb.mp.
2. pustulosis palmaris et plantaris.ti,ab.	35. narrow band ultraviolet.mp.
3. (pustulosis and palm and soles).ti,ab.	36. psoralen ultraviolet a.mp.
4. palmoplantar* pustulosis.ti,ab.	37. psoralen uva.mp.
5. 1 or 2 or 3 or 4	38. Laser therap*.mp. or Laser Therapy/
6. Urea/ or Urea*.mp.	39. Ciclospori*.mp. or Cyclosporine/
7. uric acid.mp. or Uric Acid/	40. cyclospor*.mp.
8. salicyl* acid.mp. or Salicylic Acid/	41. fumar*.mp. or exp Fumarates/
9. Calcineu* inhibito*.mp. or Calcineurin Inhibitors/	42. fumaderm.mp.
10. Tacrolimus/ or Pimecrolim*.mp.	43. dimethylfumara*.mp.
11. dithranol*.mp. or Anthralin/	44. fae.ti,ab.
12. Cortisone/ or cortiso*.mp.	45. dmf.ti,ab.
13. Betamethasone/ or Betametha*.mp.	46. exp Methotrexate/ or MTX.mp.
14. mometaso*.mp. or Glucocorticoids/ or Mometasone Furoate/	47. methotrexa*.mp.
15. Retinoids/ or tazarot*.mp.	48. amethopterin.mp.
16. coal tar.mp. or Coal Tar/ 17. vit d3.mp or Cholecalciferol/	49. mexate.mp.
18. calcipotrio*.mp.	50. acitretin.mp. or Acitretin/
19. tacalcito*.mp.	51. Retinoids/
20. Calcitriol/ or calcitrio*.mp.	52. Phosphodiesterase 4 Inhibitors/ or apremilast.mp.
21. phototherap*.mp. or exp Phototherapy/	53. cdp571.mp.
22. PUVA Therapy/ or Photochemotherapy/ or PUVA.mp.	54. (etanercep* or enbrel).mp. or Etanercept/
23. exp Ultraviolet Therapy/ or UV-B therap*.mp.	55. (Infliximab* or remicade).mp. or Infliximab/
24. photodynamic therap*.mp.	56. ustekinumab.mp. or Ustekinumab/
25. photochemotherap*.mp.	57. (briakinumab or ABT-874).mp.
26. light therap*.mp.	58. CNTO 1275.mp.
27. photoradiation therap*.mp.	59. stelara.mp.
28. BBUVB.mp.	60. secukinumab.mp.
29. NBUVB.mp.	61. guselkumab.mp.
30. BB-UVB.mp.	62. adalimumab*.mp. or Adalimumab/
31. NB-UVB.mp.	63. (d2e7 or humira).mp.
32. broad band uvb.mp.	64. exp Antibodies, Monoclonal/
33. broad band ultraviolet.mp.	65. monoclonal antibod*.mp.

65. monoclonal antibod*.mp.

66. exp Interleukin-23/ or exp Interleukin-12/
67. brodalumab.mp.
68. ixekizumab.mp.
69. (tumor necrosis factor-alpha or tumour necrosis factor-alpha).mp.
70. anti tnf.mp.
71. (tumor necrosis factor antibod* or tumour necrosis factor antibod*).mp.
72. (antitumor necrosis factor or antitumour necrosis factor).mp.
73. (anti tumor necrosis factor or anti tumour necrosis factor).mp.
74. (tnf antibod* or tnf alpha antibod*).mp.
75. climate therap*.mp. or Climatotherapy/
76. Psychotherapy/ or psychosocial therap*.mp.
77. exp Tumor Necrosis Factor-alpha/
78. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 79. 5 and 78 80. Diabetes mellitus.mp. or Diabetes mellitus/ 81. Diabetes Mellitus, Type 1/ or Diabetes Mellitus, Type 2/ or diabetes mellitus type 1.mp. 82. DM.ti,ab. 83. (Type 1 diabetes mellitus or type 2 diabetes mellitus).ti,ab. 84. (type 1 DM or type 2 DM).ti,ab. 85. 80 or 81 or 82 or 83 or 84 86. 79 and 85

Excluded full-texts for the review on psoriasis and diabetes mellitus:

A. Abdelmaksoud	2019	off-topic
K. Abuabara	2010	off-topic
T. Ahern	2013	off-topic
E. Akasaka	2013	no relevant outcomes
J. Alcantara-Gonzalez	2012	study design
N. Al-Mutairi	2014	double
M. Amy de la Breteque	2017	off-topic
Anonymous	1973	no relevant outcomes
Anonymous	2018	no relevant outcomes
Y. Arakawa	2019	off-topic
A. Armstrong and E. Levi	2017	study design
A. W. Armstrong	2013	no relevant outcomes
D. Arps	2013	study design
F. Augey	2004	study design
R. S. Azfar	2012	off-topic
R. S. Azfar	2012	off-topic
P. Babakinejad	2018	off-topic
P. Balasubramaniam	2004	off-topic
J. Belzunegui	2001	off-topic
I. Ben-Skowronek	2013	off-topic
T. Bhutani	2013	no relevant outcomes
P. B. Bookstaver	2008	study design
P. B. Bookstaver	2008	study design
Y. B. Brauchli	2008	off-topic
E. I. Brokalaki	2012	study design
B. A. Buckingham and C. I. Sandborg	2000	off-topic
S. O. Bulic	2018	study design
S. Burillo-Martinez	2016	off-topic
R. E. Burns and F. W. Whitehouse	1973	off-topic
A. Campanati	2013	off topic
T. M. Capusan	2018	study design
A. Carija	2019	study design
J. C. Cather	2017	no relevant outcomes

H. H. Chen	2017	off-topic
Y. J. Chen	2012	no relevant outcomes
D. Cheung and M. Bryer-Ash	2009	study design
Y. Y. Chin	2013	no relevant outcomes
C. H. Chu and C. Davis	2017	study design
L. Costa	2014	off-topic
W. H. Crown	2004	no relevant outcomes
M. Daghem and D. Newby	2018	off-topic
E. Dantes	2018	study design
C. De Simone	2010	study design
T. Dehpouri	2019	off-topic
K. Eisendle and P. Fritsch	2005	study design
J. El Khalifa	2013	study design
H. Escande	2013	no relevant outcome
M. Esposito	2008	study design
M. Esposito	2019	off-topic
R. Eswaran	2018	study design
J. Fleming and S. Bashir	2012	study design
S. Foster	2015	no relevant outcomes
P. Freire	2016	off-topic
S. Gerdes	2008	no relevant outcomes
P. Gisondi	2013	off-topic
P. Gisondi	2013	off-topic
P. Gisondi	2011	no relevant outcomes
P. Gisondi	2013	no relevant outcomes
P. Gisondi	2008	off-topic
P. Gisondi	2019	off-topic
A. B. Gottlieb	2017	off-topic
C. E. M. Griffiths	2017	off-topic
E. Guevara	2015	study design
W. Gulliver and S. Gulliver	2018	study design
W. P. Gulliver	2016	off-topic
R. Gupta	2014	no relevant outcomes

K. A. Haitz and R. E. Kalb	2007	off-topic
K. M. Halprin	1982	off-topic
P. Helliwell	2018	off-topic
C. Herz	2017	off-topic
R. Hillson	2019	off-topic
Y. Hongo	2017	study design
Y. Hongo	2017	study design
W. D. Hoover	2007	study design
W. Hussain	2008	study design
S. Imafuku	2016	off-topic
S. Imafuku	2016	off-topic
I. Y. Iskandar	2015	no relevant outcomes
T. Ito	2018	off-topic
A. Jacobi	2013	no relevant outcomes
E. C. Johns and R. M. Reynolds	2019	study design
R. Kalb	2015	double
R. E. Kalb	2015	double
A. Kimball	2009	double
A. B. Kimball	2014	off-topic
A. B. Kimball	2008	no relevant outcomes
B. Kirby	2013	double
M. Kobayashi	2018	study design
K. Kofoed	2012	off-topic
M. Kojanova	2017	no relevant outcomes
A. J. Krentz and P. S. Friedmann	2006	off-topic
J. Lachaine	2011	off-topic
C. P. Lee and B. Bt Khalid	2015	off-topic
J. J. Lee	2011	study design
M. S. Lee	2014	off-topic
M. S. Lee	2014	off-topic
O. Leonard	2012	study design (n < 100)
C. Leonardi	2015	no relevant outcomes
C. Leonardi	2019	off-topic

C. H. Loo	2015	no relevant outcomes
S. K. F. Loo	2010	study design
A. Lopez-Ferrer	2013	no relevant outcome
M. T. A. Loste	2019	off-topic
M. Lynch	2017	study design
M. Lynch	2017	off-topic
T. Mabuchi	2013	off-topic
A. W. L. Macewen	2011	study design
A. D. Maderal	2018	study design
D. A. Malatjalian	1996	no relevant outcome
V. Manfreda	2019	off-topic
P. Mansueto	2011	study design
P. Mansueto	2012	study design
S. Mantravadi	2018	study design
M. Marra	2007	off-topic
C. E. Martinez	2017	study design
C. E. Martinez	2017	study design
E. Martinez-Abundis	2007	off-topic
C. Martinez-Peinado	2016	study design
T. A. Maurer	1994	study design
A. Menter	2010	double
A. Menter	2017	no relevant outcome
A. Michalska-Bankowska	2019	study design (n < 100)
A. Michalska-Bankowska	2018	no relevant outcomes
A. Michalska-Bankowska	2019	off-topic
G. H. Millward-Sadler and T. J. Ryan	1974	study design
R. Mittal	2009	off-topic
H. Miyachi	2017	off-topic
H. Miyachi	2017	off-topic
A. Morita	2018	off-topic
U. Mrowietz	2009	no relevant outcomes
N. Mumoli	2014	study design
T. Nakamura-Wakatsuki and T. Yamamoto	2014	off-topic

T. Narang	2012	study design (n < 100)
T. Nishioka	2012	off-topic
D. Norris	2017	off-topic
D. Norris	2017	double
R. O'Connor	2015	off-topic
E. Ojaimi	2012	off-topic
Y. Okubo	2019	off-topic
E. Papadavid	2010	off-topic
K. Papp	2018	off-topic
S. Parisi	2019	off-topic
L. Patricia	2014	no relevant outcomes
P. Patro and V. Agarwal	2018	off-topic
C. M. Peinado	2016	study design
A. Perez-Plaza	2017	off-topic
E. C. Pfeifer	2017	study design
E. C. Pfeifer	2017	study design
S. Piel and J. Dissemond	2008	study design
T. Pina Murcia	2014	off topic
T. Pina	2015	off-topic
T. Pina	2015	off-topic
M. Pirowska	2019	off-topic
L. Puig	2010	no relevant outcomes
L. Puig	2015	off-topic
J. Qiang	2016	no relevant outcomes
E. Rallis and V. Anyfantakis	2008	study design
B. Rao	2015	study design
K. Reich	2013	no relevant outcomes
K. Reich	2013	no relevant outcomes
P. Rimbaud and J. Meynadier	1968	off-topic
C. Riquelme-Mc Loughlin	2018	study design
H. H. Roenigk Jr	1971	off-topic
C. C. Romero	2010	no relevant outcomes
R. M. Romero-Jimenez	2018	no relevant outcome

P. Rosenberg	2007	study design (n < 100)
L. S. Sauter	1971	off-topic
L. Selvarajah	2016	study design
A. Shahbaz	2017	no relevant outcomes
A. Shahbaz	2017	no relevant outcomes
J. Shapiro	2007	off-topic
V. Singh	2019	off-topic
V. M. Smith and V. Goulden	2014	study design
D. H. Solomon	2011	off-topic
B. Strober	2017	off-topic (no DM)
B. Strober	2018	no relevant outcomes
J. Takeshita	2015	no relevant outcomes
M. Tokuyama	2019	off-topic
H. Trattner	2017	off-topic
H. Trattner	2017	no relevant outcomes
S. Troyanova-Slavkova and L. Kowalzick	2019	study design
E. Tula	2017	double
Y. Umezawa	2015	study design
F. Ursini	2010	study design
D. A. Vekic and J. W. Frew	2018	off-topic
R. Vender	2013	off-topic
C. G. Wambier	2009	study design
K. C. Wei and P. C. Lai	2015	off-topic
J. Wu	2012	double
J. J. Wu and K. Y. T. Poon	2013	no relevant outcome
J. J. Wu and T. F. Tsai	2008	study design
K. Xu	2010	study design
T. Yamaguchi	2017	off-topic
T. Yamaguchi	2017	off-topic
Z. Yao	2018	off-topic
B. Yazdani-Biuki	2006	off-topic
C. M. Yeo	2009	no relevant outcomes
P. D. Yesudian	2016	no relevant outcomes

Y. Zhu	2009	no relevant outcomes
L. Zisova	2012	no relevant outcomes

References

AL-MUTAIRI, N. & SHABAAN, D. 2016. Effects of tumor necrosis factor alpha inhibitors extend beyond psoriasis: insulin sensitivity in psoriasis patients with type 2 diabetes mellitus. *Cutis,* 97**,** 235-41.

BLAUVELT, A., REICH, K., TSAI, T. F., TYRING, S., VANACLOCHA, F., KINGO, K., ZIV, M., PINTER, A., VENDER, R., HUGOT, S., YOU, R., MILUTINOVIC, M. & THACI, D. 2017. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: Results from the CLEAR study. *J Am Acad Dermatol,* 76**,** 60-69.e9.

HIGGINS JPT, S. J., SAVOVIĆ J, PAGE MJ, HRÓBJARTSSON A, BOUTRON I, REEVES B, ELDRIDGE S. A ; 2016. revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. *Cochrane Database of Systematic Reviews*.

HONG, J. R., LEE, Y. W., CHOE, Y. B. & AHN, K. J. 2019. Risk factors for increased serum creatinine level in patients with psoriasis treated with cyclosporine in a real-world practice. *Dermatologic Therapy,* 32 (3) (no pagination).

KALB, R. E., FIORENTINO, D. F., LEBWOHL, M. G., TOOLE, J., POULIN, Y., COHEN, A. D., GOYAL, K., FAKHARZADEH, S., CALABRO, S., CHEVRIER, M., LANGHOLFF, W., YOU, Y. & LEONARDI, C. L. 2015. Risk of Serious Infection With Biologic and Systemic Treatment of Psoriasis: Results From the Psoriasis Longitudinal Assessment and Registry (PSOLAR). *JAMA Dermatology,* 151**,** 961-9.

KIMBALL, A. B., BENSIMON, A. G., GUERIN, A., YU, A. P., WU, E. Q., OKUN, M. M., BAO, Y., GUPTA, S. R. & MULANI, P. M. 2011. Efficacy and safety of adalimumab among patients with moderate to severe psoriasis with co-morbidities: Subanalysis of results from a randomized, double-blind, placebo-controlled, phase III trial. *American Journal of Clinical Dermatology,* 12**,** 51-62.

KOENIG, A. S., SZUMSKI, A., PEDERSEN, R. & ROBERTSON, D. H. 2011. Impact of etanercept therapy on glycemic control in a cohort of psoriatic patients: The pristine trial

Arthritis and Rheumatism. Conference: Annual Scientific Meeting of the American College of Rheumatology and Association of Rheumatology Health Professionals, 63.

LANGLEY, R. G., ELEWSKI, B. E., LEBWOHL, M., REICH, K., GRIFFITHS, C. E., PAPP, K., PUIG, L., NAKAGAWA, H., SPELMAN, L., SIGURGEIRSSON, B., RIVAS, E., TSAI, T. F., WASEL, N., TYRING, S., SALKO, T., HAMPELE, I., NOTTER, M., KARPOV, A., HELOU, S. & PAPAVASSILIS, C. 2014. Secukinumab in plaque psoriasis--results of two phase 3 trials. *N Engl J Med,* 371**,** 326-38.

MENTER, A., TYRING, S. K., GORDON, K., KIMBALL, A. B., LEONARDI, C. L., LANGLEY, R. G., STROBER, B. E., KAUL, M., GU, Y., OKUN, M. & PAPP, K. 2008. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. *J Am Acad Dermatol,* 58**,** 106-15.

MURAD, M. H., ASI, N., ALSAWAS, M. & ALAHDAB, F. 2016. New evidence pyramid. *Evidence Based Medicine,* 21**,** 125-127.

OCEBM LEVELS OF EVIDENCE WORKING GROUP & * OCEBM LEVELS OF EVIDENCE WORKING GROUP = JEREMY HOWICK, I. C. J. L. L., PAUL GLASZIOU, TRISH GREENHALGH, CARL HENEGHAN, ALESSANDRO LIBERATI, IVAN MOSCHETTI, BOB PHILLIPS, HAZEL THORNTON, OLIVE GODDARD AND MARY HODGKINSON. 2011. "The Oxford Levels of Evidence 2". Available: https://www.cebm.net/2016/05/ocebm-levels-of-evidence/ [Accessed 10 August 2018].

PINTER, A., GERDES, S., PAPAVASSILIS, C. & REINHARDT, M. 2019. Characterization of responder groups to secukinumab treatment in moderate to severe plaque psoriasis. *Journal of Dermatological Treatment.*

STERNE, J. A., HERNÁN, M. A., REEVES, B. C., SAVOVIĆ, J., BERKMAN, N. D., VISWANATHAN, M., HENRY, D., ALTMAN, D. G., ANSARI, M. T., BOUTRON, I., CARPENTER, J. R., CHAN, A.-W., CHURCHILL, R., DEEKS, J. J., HRÓBJARTSSON, A., KIRKHAM, J., JÜNI, P., LOKE, Y. K., PIGOTT, T. D., RAMSAY, C. R., REGIDOR, D., ROTHSTEIN, H. R., SANDHU, L., SANTAGUIDA, P. L., SCHÜNEMANN, H. J., SHEA, B., SHRIER, I., TUGWELL, P., TURNER, L., VALENTINE, J. C., WADDINGTON, H., WATERS, E., WELLS, G. A., WHITING, P. F. & HIGGINS, J. P. 2016. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ,* 355.

STROHAL, R., PUIG, L., CHOUELA, E., TSAI, T. F., MELIN, J., FREUNDLICH, B., MOLTA, C. T., FUIMAN, J., PEDERSEN, R. & ROBERTSON, D. 2013. The efficacy and safety of etanercept when used with as-needed adjunctive topical therapy in a randomised, double-blind study in subjects with moderate-to-severe psoriasis (the PRISTINE trial). *J Dermatolog Treat,* 24**,** 169-78.

WU, J. J., LIU, L., ASGARI, M. M., CURTIS, J. R., HARROLD, L., SALMAN, C. & HERRINTON, L. J. 2014. Initiation of TNF inhibitor therapy and change in physiologic measures in psoriasis. *Journal of the European Academy of Dermatology & Venereology,* 28**,** 1380-7.

WU, J. J., ROWAN, C. G., BEBCHUK, J. D. & ANTHONY, M. S. 2015. No association between TNF inhibitor and methotrexate therapy versus methotrexate in changes in hemoglobin A1C and fasting glucose among psoriasis, psoriatic arthritis, and rheumatoid arthritis patients. *Journal of Drugs in Dermatology: JDD,* 14**,** 159-66.

Appendix 7 Viral Hepatitis

Hepatitis: Systematic review of the evidence on psoriasis treatment and viral hepatitis

The work was conducted as part of a doctoral thesis by Rhea Jakubzyk, who gave permission to print the work here. Passenges here may be identical to her thesis.

Eligibility criteria

We included all studies on adult patients with a clinical diagnosis of psoriasis and a concomitant hepatitis B or C being treated for psoriasis. Viral hepatitis was defined as positive serological or virological marker for hepatitis B virus (HBV) or hepatitis C virus (HCV) before onset of the psoriasis treatment.

The interventions were specified to be topical treatment (urea, salicylic acid, calcineurin-inhibitors (pimecrolimus, tacrolimus), dithranol, corticosteroids (betamethasone, mometasonfuroat), tazaroten, coal tar, vitamin D3 derivate (calcipotriol, tacalcitol, calcitriol, calcipotriol and betamethasone) or systemic treatment (aciretin, ciclosporin, fumarates, methotrexate, apremilast) for psoriasis including biologicals (Anti TNF-alpha: etanercept, infliximab, adalimumab; Anti-IL12/23: ustekinumab; Anti-IL17: secukinumab, ixekizumab, brodalumab; Anti-IL23). We included studies comparing the intervention to placebo or another treatment and those without comparator.

The following outcomes were of interest:

- Change in skin lesions based on PASI (Psoriasis Area Severity Index) or PGA (Physician Global Assessment) or another study specific assessment.
- Transaminases, viral load or other study specific outcomes
- Type and proportion of other adverse events
- Quality of life based on SF-36 (The Short Form (36) Health Survey), DLQI (Dermatology Life Quality Index) or another study specific assessment.

When possible, we evaluated the outcomes at different timings, based on what was reported in the publications (e.g. short-term, long-term).

Included were randomized controlled trials, clinical trials (with and without comparison group), cohort studies, case control studies and cross sectional studies. We used a step-wise approach for including studies (for each study drug and comparator) following the hierarchy of evidence (Murad et al., 2016).

We excluded studies on patients with psoriatic arthritis because of the different pathophysiology and treatment options.

Information sources

Three databases were searched systematically (MEDLINE Ovid from 1946, Embase Ovid from 1974 and The Cochrane Central Register of Controlled Trials (CENTRAL); updated last in January 2019). Furthermore, we examined the reference lists of included studies to identify references to relevant trials. The full search strategy is shown below.

Study selection

We screened all identified abstracts/titles for eligibility. Included titles/abstracts were then screened as full texts based on the above listed eligibility criteria.

Data collection and reporting

Endnote was used to manage all records. One reviewer performed the screening and did the data extraction using a standardized form. A second reviewer checked 50% of the data with high agreement. We recorded all full-texts excluded and the primary reason for exclusion (see below).

Data Items

The following items were extracted: Author, year of publication, country in which the study took place, study design, inclusion and exclusion criteria, baseline characteristics of the included patients, details of the interventions, details of any co-interventions, number and reasons for drop-out, type of adverse events and proportion of patients experiencing adverse events and serious adverse events, proportion of patients who experienced worsening of liver function, proportion of patients who showed an improvement in skin lesions, proportion of patients who showed an improvement in quality of life, time of assessment of endpoints and number/rate of patients assessed.

Risk of bias assessment

We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations (OCEBM Levels of Evidence Working Group and * OCEBM Levels of Evidence Working Group = Jeremy Howick, 2011). We assigned Levels of Evidence for all studies using the Center of Evidence Based Medicine Oxford recommendations (OCEBM Levels of Evidence Working Group and * OCEBM Levels of Evidence Working Group = Jeremy Howick, 2011). To assess risk of bias in randomized trials we additionally used the RoB 2.0 tool (Higgins JPT, 2016). We planned to use the ROBINS-I tool for controlled, non-randomized studies of interventions but none of these type were included (Sterne et al., 2016).

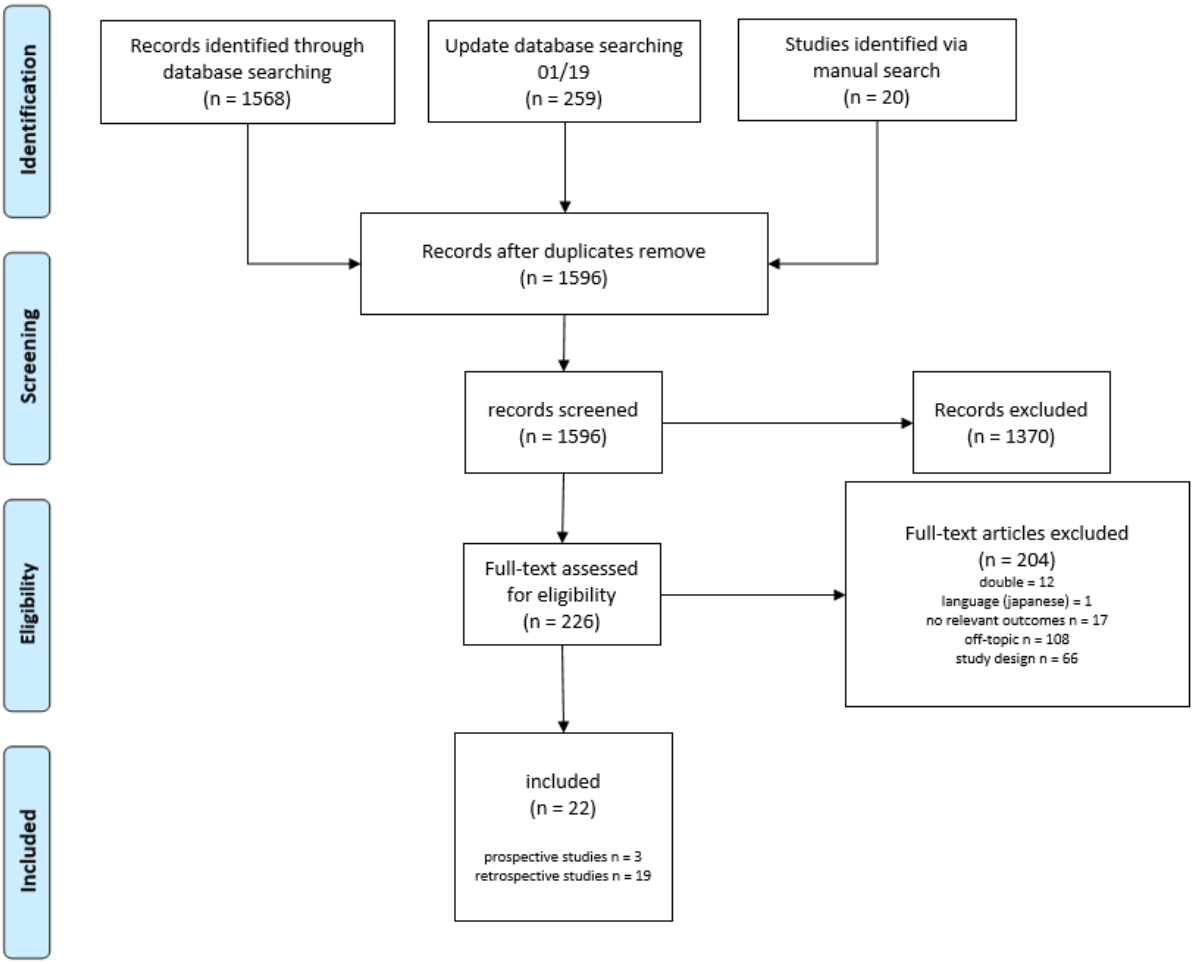
Summary measures

Data was summarized and sorted by the medication used (see Table 4 and 5). We counted the number of patients across studies reported to have liver dysfunction or HBV/HCV-reactivation during follow-up and improvement in psoriasis to provide a pragmatic overview. We summarized the results - see Table 2 and 3 - with focus on clinically relevant information (e.g. liver dysfunction or HBV/HCV-reactivation).

Results

Our search yielded 1596 citations, 22 of which fulfilled the inclusion criteria (January 2019; see study selection flow chart). Three prospective studies (Ting et al., 2018, Chiu et al., 2018, AlMutairi and Abouzaid, 2018), two studies based on registry data (Sanz-Bueno et al., 2015, Tang et al., 2018) and 17 retrospective studies (Cho et al., 2012, Nosotti et al., 2010, Cassano et al., 2011, Hsieh et al., 2018, Pereira et al., 2018, Siegel et al., 2017, Piaserico et al., 2017a, Chiu et al., 2013, Fotiadou et al., 2011, Garavaglia and Altomare, 2010, Morisco et al., 2014, Navarro et al., 2013, Piaserico et al., 2017b, Snast et al., 2017, Navarro et al., 2014, Prignano et al., 2011, Di Nuzzo et al., 2013) were included.

No studies on aciretin, apremilast, brodalumab, ciclosporin, fumarates, guselkumab, ixekizumab, risankizumab and tildrakizumab were identified that reported outcomes for viral hepatitis.



Based on the Center of Evidence Based Medicine Oxford recommendations all references included were rated level 3 (Ting et al., 2018, Chiu et al., 2018, AlMutairi and Abouzaid, 2018, Cho et al., 2012, Nosotti et al., 2010, Cassano et al., 2011, Hsieh et al., 2018, Pereira et al., 2018, Siegel et al., 2017, Piaserico et al., 2017a, Chiu et al., 2013, Fotiadou et al., 2011, Garavaglia and Altomare, 2010, Morisco et al., 2014, Navarro et al., 2013, Piaserico et al., 2017b, Snast et al., 2017, Navarro et al., 2014, Prignano et al., 2011, Di Nuzzo et al., 2013, Sanz-Bueno et al., 2015, Tang et al., 2018, OCEBM Levels of Evidence Working Group and * OCEBM Levels of Evidence Working Group = Jeremy Howick, 2011). Results of the additional assignment for prospective randomized studies are shown in Table 1 (Chiu et al., 2018, AlMutairi and Abouzaid, 2018, Higgins JPT, 2016).

Abbreviation: ⊕ = high risk of bias ? = unknown risk of bias ⊖ = low risk of bias	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Author (Year)						
Al Mutairi, N. and Abouzaid, H.A. (2018)	⊕	⊕	⊕	⊖	⊖	⊕
Chiu H. Y. et al. (2018)I	⊕	⊕	⊕	⊖	⊖	⊕

RISK OF BIAS – PROSPECTIVE RANDOMIZED STUDIES

Data for overall 1128 patients with psoriasis and viral hepatitis was extracted. Of those, 854 patients suffered from hepatitis B infection and 274 from hepatitis C infection. Most of the included studies reported individual patient data. The tables below are providing detailed information, sorted by medication used.

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
										AST mean±SD		ALT mean±SD						
								Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Base-line (n)	Eof (n)			
		ADA																
Piaserico, S et al. (2017)[II]	Italy	17	ADA	27*	50.8±12.5	35.3	/	21.2±6.9	16/17	39±25.4	40.4±25	39.7±27.8	44.9±30.4	0	0	LAM[1] (8/17) LAM/ENT[1] (1/17)	0	/
Fotiadou, C. et al. (2011)[II]	Greece	3	ADA	12±3	53.7± 10.6	33.3	6-24	14.1±2	3/3	19.3±2.1	20.7±1.2	21±2.6	21.3±2.5	0	0	none	0	/
Nosotti, L. et al. (2010)[II]	Italy	3	ADA	9.1±3.7	54±7.2	33.3	/	12.1±13.7	/	13±1.7	18.7±4.2	unchanged	unchanged	0	0	none	0	/
Navarro, R. et al. (2014)[II]	Spain	2	ADA	11 26	74 68	50	/	/		17 9	19 21	20 14	20 43	/		none	0	/
Snast, I. et al. (2017)[II]	Israel	2	ADA	12 72	55 69	0	63.7*	26.1 BSA 50	2/2 PASI50	35 19	29 34	34 24	42 14	0	0	none	0	Pneumonia (1/2)
Cho, Y.T. et al. (2012)[II]	Taiwan	1	ADA	27	44	0	14	/		15	46	22	34	0	0	none	0	none
		ETA																
Prignano, F. et al. (2011)[II]	Italy	11	ETA	8.6*	61.4*	27.3	7.3	/		unchanged				0	0	none	0	/
Snast, I. et al. (2017)[II]	Israel	8	ETA	55.2±46.3	57.3±12.2	37.5	63.7*	19.8±2.7 BSA 50 (4/8)	8/8 PASI50	27.6±16.8	22.2±7.2	24±9.2	19.5±8.5	0	0	LAM[2] (1/8)	0	none
Navarro, R. et al. (2014)[II]	Spain	7	ETA	28.7±20.7	60.6±15.4	28.6	/	/		34.9±14.9	34.7±21.4	44±23.4	32.6±19.6	/		none	0	/
Cho, Y.T. et al. (2012)[II]	Taiwan	6	ETA	24.8±12.7	42.6±4.1	16.7	31.3±13	/		34.5±26.7	35.5±8.2	33.3±24.6	47±28.9	2	2	LAM[2] (1/6) LAM/ENT[2] (1/6)	3/6	none
Nosotti, L. et al. (2010)[II]	Italy	4	ETA	10.5±5.7	51.3±5.7	0	/	7.4±4.6	/	23.5±3.1	28.3±5.7	unchanged	unchanged	0	0	LAM[2] (1/4)	0	/
Fotiadou, C. et al. (2011)[II]	Greece	3	ETA	12.1±5.9	49.7±14	66.7	6-24	12.1±2.2	3/3	17.3±1.5	18.3±1.5	20.3±3.1	22.7±3.2	0	0	LAM[2] (1/3)	0	/
Navarro, R. et al. (2013)[II]	Spain	3	ETA	27±19	43.7±13	33.3	25*	19.7±4.8	2/3 PASI50	28.3±4	44.3±14.6	46.3±3	45.7±13.7	1	0	ADE/ENT[2] (1/3) LAM[2] (2/3)	0	none

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
										AST mean±SD		ALT mean±SD						
								Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Base-line (n)	Eof (n)			
		IFX																
Navarro, R. et al. (2014)[II]	Spain	4	IFX	25.5±10.3	60.5±10	25	/		/	28.5±8.3	30.8±15.2	30.3±14.8	19.8±8.7		/	none	0	/
Fotiadou, C. et al. (2011)[II]	Greece	1	IFX	10	48	100	6-24	20.2	1/1	25	30	31	40	0	0	none	0	/
Navarro, R. et al. (2013)[II]	Spain	1	IFX	37	36	100	25*	22.2	0	42	52	64	62	0	0	LAM[2]	0	none
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	370	MTX	/	42.6±13.2	28	50.4 ±38.4		/			/			/	48/370	/	Liver cirrhosis (15/370)[3]
		SEC																
Chiu H. Y. et al. (2018)[I]	Taiwan	25	SEC	7.7 ± 3.8	49.7 ± 8.6	16	9.1 ± 3.9	13.4 ± 8.2	/		/	43.7±42.2	/		/	3/25[1]	6/25	Hepatic cancer
		24		8.7 ± 3.7	54.7 ± 13.4	25	9.2 ± 3.7	20.1 ± 8.3				41.1 ± 28.0				11/24[1]	1/24	/
		UST																
Ting, S. W. et al. (2018)[I]	Taiwan	54	UST	/	47*	16.7	24*		/			"none had liver failure"				ENT[1] (1/54) LAM[2] (1/54)	3/48	/
Hsieh, T. Y. et al. (2018)[II]	Taiwan	75	UST	/	/	/	24.7*		/			/			/	unknown[2] (2/75)	2/75	/
Chiu, H.Y. et al. (2013)[II]	Taiwan	14	UST	9.4±9	45.5±7.6	28.6	10.4*	/	5/14			unchanged		/	"increased" (4/14)	ENT[2] (4/14)	2/14	/
Piaserico, S. et al. (2017)	Italien	5	UST	57.2±13.9	55.4±16.5	20	57		/	28.8±11.6	31.8±7.9	31.2±16.2	41.8±19	0	0	LAM[1] (4/5)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	UST	7	56	0	25*	17.6	1/1 PASI50	32	16	35	15	1/1	0	ENT[2]	0	none

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
										AST mean±SD		ALT mean±SD						
								Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Base-line (n)	Eof (n)			
		IFX																
Navarro, R. et al. (2014)[II]	Spain	4	IFX	25.5±10.3	60.5±10	25	/		/	28.5±8.3	30.8±15.2	30.3±14.8	19.8±8.7		/	none	0	/
Fotiadou, C. et al. (2011)[II]	Greece	1	IFX	10	48	100	6-24	20.2	1/1	25	30	31	40	0	0	none	0	/
Navarro, R. et al. (2013)[II]	Spain	1	IFX	37	36	100	25*	22.2	0	42	52	64	62	0	0	LAM[2]	0	none
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	370	MTX	/	42.6±13.2	28	50.4 ±38.4		/			/			/	48/370	/	Liver cirrhosis (15/370)[3]
		SEC																
Chiu H. Y. et al. (2018)[I]	Taiwan	25	SEC	7.7 ± 3.8	49.7 ± 8.6	16	9.1 ± 3.9	13.4 ± 8.2	/		/	43.7±42.2	/		/	3/25[1]	6/25	Hepatic cancer
		24		8.7 ± 3.7	54.7 ± 13.4	25	9.2 ± 3.7	20.1 ± 8.3				41.1 ± 28.0				11/24[1]	1/24	/
		UST																
Ting, S. W. et al. (2018)[I]	Taiwan	54	UST	/	47*	16.7	24*		/			"none had liver failure"				ENT[1] (1/54) LAM[2] (1/54)	3/48	/
Hsieh, T. Y. et al. (2018)[II]	Taiwan	75	UST	/	/	/	24.7*		/			/			/	unknown[2] (2/75)	2/75	/
Chiu, H.Y. et al. (2013)[II]	Taiwan	14	UST	9.4±9	45.5±7.6	28.6	10.4*	/	5/14			unchanged		/	"increased" (4/14)	ENT[2] (4/14)	2/14	/
Piaserico, S. et al. (2017)	Italien	5	UST	57.2±13.9	55.4±16.5	20	57		/	28.8±11.6	31.8±7.9	31.2±16.2	41.8±19	0	0	LAM[1] (4/5)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	UST	7	56	0	25*	17.6	1/1 PASI50	32	16	35	15	1/1	0	ENT[2]	0	none

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I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
								Baseline mean±SD	e.g. PASI-75 response eof (n)	AST mean±SD		ALT mean±SD		Base-line (n)	Eof (n)			
										Baseline	Eof	Baseline	Eof					
		> than one treatment																
Cassano N. et al. (2010)[II]	Italy	62	ETA (44) ADA (10) IFX (8)	27.8* 19* 28.8*	54*	32.3	55	15.3 (10.2-39.9)	/		"normal value"			"undetectable"		LAM[2] (1/62)	0	/
Morisco, F. et al. (2014)[II]	Italy	23 36	ADA, ETA, UST, IFX, MTX, CsA	/	66±10.6 52±12.4	56.5 25	/	/		/	unchanged	27±2.3 24±3.2	unchanged	0	0	none	0	/
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	28	ADA (11) ETA (10) UST (8)	14.7±12.3 21.7±25.3 30±14.7	51±13.2	10.7	41.4 ±21.4	14.2±1.5	28/28	22 (17–25.8)	23 (12.3–28.8)	21 (17.1–26.4)	23 (14.7–25.3)	0		none	0	none
		4	ADA (3) ETA (4) UST (1)	15.4±11.7 18.5±23.6 28±11.9	49±15.6	25			4/4							LAM[2] (4/4)		
Pereira, R.et al. (2018)[II]	Portugal	26	ETA (12) ADA (8) IFX (6) >1 (13)	37.2 50.4 58.8 /	52.7±14.1	38.5	43.6 ±28.7	/		/				"undetectable"		/	0	/
Sanz-Bueno, J. (2015)[I]	Spain	20	ADA (13) ETA (7) UST (6) IFX (7)	13 16 18 22	/	25	40*	/		unchanged				0	0	none	0	/
Snast, I. et al. (2017)[II]	Israel	16	ETA (16), ADA (14), IFX (5), UST (12), SEC (3), GOL (1), ALE (1)	70.8±32.4	55.2±11.4	31.3	63.7*	23.3±8.6 BSA 50 (5/16) BSA 70 (1/16)	9/16 PASI50	22.7±5.6	21.9±8.3	21.5±7	19.3±10.7	0	0	LAM[2] (1/16)	0	Respiratory infection (1/16), myocardial infarction (1/16) erythema (2/16)

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* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis C

Author (Year)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Duration of follow-up (M) mean±SD	Severity Score (e.g. PASI)		Transaminases				Viral load		Antiviral therapy (n)	HCV reactivation (n)	Adverse envent
								Baseline mean±SD	e.g. PASI-75 response, eof (n)	AST mean±SD		ALT mean±SD		Baseline detectable (n)	Change at eof (q)			
										Baseline	Eof	Baseline	Eof					
		ADA																
Piaserico, S et al. (2017)[II]	Italy	20	ADA	40*	49.8±11.3	30	/	15.8±6.2	14/20	39.5±21.2	53.9±32.7	38±20.7	57.3±36.4	16/20	↓ 7/16 (0.7±0.3) ↑ 9/16 (8.8±17.1)	RIB[1] (1/20) IFN/RIB[1] (1/20)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	ADA	2	65	0	/	15.6	0/1	20	30	34	55	1/1	↑ (1.03)	none	0	Stroke (1/1)
		ETA																
Navarro, R. et al. (2013)[II]	Spain	12	ETA	15.5±5.9	51.5±12.8	16.7	/	17.8±8.8	6/12	82.8±42.2	61.9±31	88.1±40.9	53.1±22.5	6/12	↓ 4/6 (0.04±0.08) ↑ 2/6 (8.2±12)	IFN/RIB[2] (3/12)	0	Respiratory Infection (1/12) HCC (2/12)
Garavaglia, M.C. et al. (2010)[II]	Italy	5	ETA	15.6±7.1	59±10.7	20	7-24	22.9±3.2	4/5	42.8±14.1	43±23.6	49±10.5	52.4±37.7	4/5	↓ 3/4 (0.64±0.5) ↑ 1/4 (1.22)	IFN/RIB[2] (1/5)	0	/
Di Nuzzo, S. et al. (2013)[II]	Italy	5	ETA	12*	60*	0	/	/		"increased" (2/5)				"unchanged"		/	0	HCC (1/5)
Snast, I. et al. (2017)[II]	Israel	3	ETA	18±9.6	57±16.6	0	22.3 (8-36)	19.5±6.7	2/3	48.3±7.6	53.7±18.6	58.7±5.7	72.3±22.9	3/3	↓ 1/3 (0) ↑ 2/3 (1.93±0.93)	none	0	none
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	174	MTX	/	50.4±12.6	36	57.6±42	/		/				/		42/174	/	Liver cirrhosis (19/174)[3]
		SEC																
Chiu, H. Y. et al. (2018)[I]	Taiwan	14	SEC	8.6 ± 3.4	53.9 ± 12.7	14.3	9.0 ± 3.9	/	"Improvement in PASI": 77.7 ± 18.5	/		48.4 ± 50.1	"no significant differences"	/	"no significant differences"	IFN/RIB[1] (4/14) DAA[2] (1/14)	1	HCC
Siegel, S. A. R. et al. (2017)[II]	USA	3	SEC	/	54-64	/	/	/		"no evidence of significant elevations"				/		/	0	/
		UST																
Chiu, H.Y. et al. (2013)[II]	Taiwan	4	UST	8±2.6	64.8±12.1	0	9.5*	/	0/4	"slightly increased" (3/4)				/	"increased" (3/4)	none	1	HCC (1/4)
		more than one treatment (n)																
Morisco, F. et al. (2014)[II]	Italy	15	ADA, ETA, UST, IFX	/	62±11.8	20	48	/		/	/	25	"unchanged"	/	"unchanged"	none	0	/
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	7	ADA (7) ETA (1)	13.7±10.4 20	54±12.9	40	41.4±21.4	/	7/7	22 (17–25.8)	21 (17.1–26.4)	23 (12.3–28.8)	23 (14.7–25.3)	"detectable level" (2/4)	"detectable level" (2/4)	/	0	none
Prignano, F. et al. (2011)[II]	Italy	5	ADA (2) ETA (3)	6 8.6	50.4*	25	7.3	/		"unchanged"				"unchanged"		none	0	/
Navarro, R. et al. (2013)[II]	Spain	5	ADA (3) ETA (5) UST (1) IFX (1)	6.7±3.8 15.6±16.2 17 8	39.8±11.3	0	/	14.6±8.3	2/5	110±78.9	145±114.7	106.6±68.1	107.9±46.1	2/5	↓ 1/2 (0) ↑ 1/2 (1.57)	none	0	none
Snast, I. et al. (2017)[II]	Israel	1	ETA ADA	36	78	0	22.3*	BSA 50	1/1	68	32	74	32		/	none	0	none

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ADA = Adalimumab; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; DAA = Direct acting antivirals; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab; HCC = Hepatocellular Carcinoma; HCV = Hepatitis C Virus; IFN = Interferon; IFX = Infliximab; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; RIB = Ribavirin; SEC = Secukinumab; UST = Ustekinumab

Search strategy for the review on psoriasis and viral hepatitis (Embase Ovid)

1. exp Psoriasis/ or Psoria*.mp.
2. pustulosis palmaris et plantaris.ti,ab.
3. (pustulosis and palm and soles).ti,ab.
4. palmoplantar* pustulosis.ti,ab.
5. 1 or 2 or 3 or 4
6. Urea/ or Urea*.mp.
7. uric acid.mp. or Uric Acid/
8. salicyl* acid.mp. or Salicylic Acid/
9. Calcineu* inhibito*.mp. or Calcineurin Inhibitors/
10. Tacrolimus/ or Pimecrolim*.mp.
11. dithranol*.mp. or Anthralin/
12. Cortisone/ or cortiso*.mp.
13. Betamethasone/ or Betametha*.mp.
14. mometaso*.mp. or Glucocorticoids/ or Mometasone Furoate/
15. Retinoids/ or tazarot*.mp.
16. coal tar.mp. or Coal Tar/ 17. vit d3.mp or Cholecalciferol/
18. calcipotrio*.mp.
19. tacalcito*.mp.
20. Calcitriol/ or calcitrio*.mp.
21. phototherap*.mp. or exp Phototherapy/
22. PUVA Therapy/ or Photochemotherapy/ or PUVA.mp.
23. exp Ultraviolet Therapy/ or UV-B therap*.mp.
24. photodynamic therap*.mp.
25. photochemotherap*.mp.
26. light therap*.mp.
27. photoradiation therap*.mp.
28. BBUVB.mp.
29. NBUVB.mp.
30. BB-UVB.mp.
31. NB-UVB.mp.
32. broad band uvb.mp.
33. broad band ultraviolet.mp.
34. narrow band uvb.mp.
35. narrow band ultraviolet.mp.
36. psoralen ultraviolet a.mp.
37. psoralen uva.mp.
38. Laser therap*.mp. or Laser Therapy/
39. Ciclospori*.mp. or Cyclosporine/
40. cyclospor*.mp.
41. fumar*.mp. or exp Fumarates/
42. fumaderm.mp.
43. dimethylfumara*.mp.
44. fae.ti,ab.
45. dmf.ti,ab.
46. exp Methotrexate/ or MTX.mp.
47. methotrexa*.mp.
48. amethopterin.mp.
49. mexate.mp.
50. acitretin.mp. or Acitretin/
51. Retinoids/
52. Phosphodiesterase 4 Inhibitors/ or apremilast.mp.
53. cdp571.mp.
54. (etanercep* or enbrel).mp. or Etanercept/
55. (Infliximab* or remicade).mp. or Infliximab/
56. ustekinumab.mp. or Ustekinumab/
57. (briakinumab or ABT-874).mp.
58. CNTO 1275.mp.
59. stelara.mp.
60. secukinumab.mp.
61. guselkumab.mp.
62. adalimumab*.mp. or Adalimumab/
63. (d2e7 or humira).mp.
64. exp Antibodies, Monoclonal/
65. monoclonal antibod*.mp.
66. exp Interleukin-23/ or exp Interleukin-12/
67. brodalumab.mp.
68. ixekizumab.mp.
69. (tumor necrosis factor-alpha or tumour necrosis factor-alpha).mp.

70. anti tnf.mp.
71. (tumor necrosis factor antibod* or tumour necrosis factor antibod*).mp.
72. (antitumor necrosis factor or antitumour necrosis factor).mp.
73. (anti tumor necrosis factor or anti tumour necrosis factor).mp.
74. (tnf antibod* or tnf alpha antibod*).mp.
75. climate therap*.mp. or Climatotherapy/
76. Psychotherapy/ or psychosocial therap*.mp.
77. exp Tumor Necrosis Factor-alpha/
78. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77
79. 5 and 78
80. exp Hepatitis/ or Hepatit*.mp.
81. chronic hepatit*.mp. or exp Hepatitis, Chronic/
82. Hepatitis B/ or hepatit* b.mp.
83. HBV.ti,ab.
84. Hepatitis C, Chronic/ or Hepatitis C/ or hepatit* c.mp.
85. non a non b hepatit*.mp.
86. HCV.ti,ab.
87. hepati* d.mp.
88. Hepatitis A/ or hepatit* infection.mp.
89. HAV.ti,ab.
90. 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89
91. 79 and 90

Excluded full-texts for the review on psoriasis and viral hepatitis

A. Abuchar	2013	study design
A. J. Alcaide	2008	study design
N. AlMutairi and H. A. Abouzaid	2018	double
Anonymous	2003	off-topic
Anonymous	2016	double
E. A. Antoniou	2016	off-topic
M. Armengot-Carbo	2013	off-topic
S. Ashraf	2013	off-topic
S. Aslanidis	2007	off-topic
G. Babino	2013	study design
F. Bartalesi	2013	study design
S. E. Behnam	2010	study design
G. Berge	1970	off-topic
S. L. Bevans	2018	study design
S. L. Bevans	2018	study design
E. Bjornsson	2015	off-topic
M. J. Boffa	1995	off-topic
L. Bomm	2011	study design
C. Bonifati	2016	study design
W. W. Bottomley	1990	study design
D. E. Branisteanu	2010	no relevant outcomes
V. Brazzelli	2012	off-topic
N. P. Burrows	1995	off-topic
M. V. Cannizzaro	2017	study design
S. C. Carneiro	2008	off-topic
N. Cassano and G. A. Vena	2008	off-topic
I. Cavazzana	2008	off-topic
R. Cecchi and L. Bartoli	2006	study design
P. Cetkovska	2015	off-topic
M. Chima and M. Lebwohl	2018	off-topic
A. Chiricozzi	2018	off-topic
Y. Chiu	2018	no relevant outcomes
Y. M. Chiu	2018	no relevant outcomes
Y. M. Chiu	2017	no relevant outcomes
Y. M. Chiu	2017	off-topic
E. Chouela	1996	off-topic
C. H. Chu and C. Davis	2017	study design
W. T. Clarke	2018	off-topic
M. H. Collazo	2008	study design
A. Conde-Taboada	2009	study design
S. Couderc	2015	off-topic
M. S. Dag	2013	off-topic
B. Dahmani and O. Boudghene Stambouli	2013	off-topic
L. J. Dang	2014	off-topic
C. De Simone	2006	study design
V. Di Lernia and E. Guareschi	2010	off-topic
V. Di Lernia	2013	study design
S. Di Nuzzo	2016	study design
A. M. Downs and M. G. Dunnill	2000	off-topic
H. V. Dubin and E. R. Harrell	1970	off-topic
C. Efe	2010	off-topic
K. Eisendle and P. Fritsch	2005	study design
A. A. Elfert	2017	off-topic
M. Enomoto	2018	off-topic
M. Enomoto	2018	off-topic
E. Erkek	2000	study design
M. Esposito	2017	off-topic
D. A. Fairhurst and R. Sheehan-Dare	2009	off-topic
B. Feaster	2018	study design
D. J. Filip	1971	off-topic
A. Finet	2016	off-topic
B. Foroncewicz	2014	off-topic
C. Fotiadou	2018	study design

M. Galeazzi	2007	study design	V. Manfreda	2019	off-topic
R. K. Gandhi	2010	study design	R. Manfredi	2010	off-topic
I. Garcia-Doval	2012	off-topic	R. Manfredi and S. Sabbatani	2010	off-topic
E. Garcia-Lora	1993	no relevant outcomes	V. Martinez-Santana	2018	study design
			A. Mebazaa	2009	no relevant outcomes
B. Ghang	2017	study design			
A. M. Giovanna Brunasso	2012	study design	G. H. Millward-Sadler and T. J. Ryan	1974	off-topic
G. Girolomoni	2012	study design			
R. Gish	2018	study design	H. Miura	1999	study design
P. Gisondi	2009	off-topic	M. Moghoofei	2018	study design
C. Goujon	2010	off-topic	C. C. Mok	2014	off-topic
F. Heppt and M. Sticherling	2016	no relevant outcomes	S. Nakayama	2013	off-topic
			R. Nankani	2017	off-topic
F. Heppt and M. Sticherling	2017	off-topic	D. J. No	2017	double
F. Heppt and M. Sticherling	2017	study design	D. J. No	2017	study design
T. Y. Hsieh	2018	double	L. Nosotti	2011	no relevant outcomes
S. Imafuku	2007	study design			
M. Jablkowski	1997	off-topic	A. Nyfors and H. Poulsen	1977	off-topic
C. Jeon	2017	study design	R. Olteanu	2016	no relevant outcomes
C. Jeon	2017	study design			
W. Jo	2017	off-topic	R. A. O'Rourke and G. E. Eckert	1964	off-topic
J. Juan and J. J. Feld	2014	study design	K. A. Papp	2017	off-topic
W. Kaabi	2013	study design	A. Paradisi	2010	study design
T. Kaiser	2009	off-topic	D. M. Pariser and R. J. Wyles	1980	off-topic
Y. Kano	2006	off-topic	M. P. Pauly	2018	no relevant outcomes
M. Karray	2016	off-topic			
E. D. Kartal	2005	no relevant outcomes	F. Peccerillo	2018	study design
			Z. Pena	2016	off-topic
S. B. Kaushik and M. G. Lebwohl	2019	study design	L. Pescitelli	2018	study design
S. Kikuchi	2018	double	S. Piaserico	2017	double
S. Kikuchi	2018	study design	D. Piccolo	2008	study design
G. W. Kim	2013	off-topic	G. Pitarch	2007	off-topic
L. E. King Jr	1975	off-topic	Y. Poulin and G. Therien	2010	off-topic
L. E. King	1975	off-topic	F. Prestinari	2010	study design
N. Kluger	2009	off-topic	F. Prignano	2011	study design
B. Kok	2018	off-topic	F. Prignano	2009	off-topic
M. Kono	2016	language	S. Purnak and T. Purnak	2014	off-topic
J. Koskinas	2013	study design	R. Rahamimov	1995	off-topic
M. Kouba	2012	study design	A. R. Raymundo	2016	study design
C. Kreiss	2002	off-topic	S. P. Reddy	2017	study design
J. T. Kuenstner	2015	off-topic	K. Reich	2011	off-topic
C. Lasagni	2018	study design	H. Riad	2013	off-topic
R. Laurenti	2013	off-topic	F. Ricceri	2017	double
J. A. Leithead	2009	off-topic	A. G. Richetta	2009	no relevant outcomes
E. Lemmenmeier	2016	off-topic			
C. Leonardi	2019	off-topic	H. H. Roenigk, Jr.	1999	off-topic
C. Leonardi	2010	off-topic	H. H. Roenigk Jr	1971	off-topic
Z. X. Li	2012	study design	H. H. Roenigk Jr	1971	off-topic
G. Linardaki	2007	study design	C. Rokhsar	2006	study design
M. Llamas-Velasco	2015	off-topic	S. Rosner	2014	off-topic
M. Llamas-Velasco	2015	off-topic	S. Sabbatani and R. Manfredi	2010	off-topic
A. Lonardo	2001	off-topic	M. Salvi	2016	study design
R. Lovero	2017	off-topic	M. D. F. Santos Paim De Oliveira	2012	study design
C. Luan	2014	study design	J. Sanz-Bueno	2015	double
M. A. Magliocco and A. B. Gottlieb	2004	study design	R. Saraceno	2007	off-topic
			E. C. Schwaneck	2018	no relevant outcomes
N. Maki	2013	off-topic			
G. Malara	2012	no relevant outcomes	S. Siegel	2015	double
			C. H. Smith	2017	study design
I. F. Manalo	2015	study design	A. H. Solay	2018	no relevant

		outcomes
W. Sondermann	2017	off-topic
R. B. Steglich	2014	study design
R. B. Stephens and A. Cooper	1999	off-topic
H. Y. Suh	2017	off-topic
Y. Takagi	2000	study design
H. Talat	2017	off-topic
A. Tamburello	2018	off-topic
C. Taylor	2000	off-topic
N. S. Tekin	2010	study design
S. W. Ting	2018	double
J. C. Titos-Arcos	2011	off-topic
H. Tobias and R. Auerbach	1973	off-topic
E. Tula	2017	off-topic
C. H. Tung	2016	off-topic
S. Tyring	2007	off-topic
T. K. Uzuncakmak	2016	off-topic
D. Van Der Heijde	2018	off-topic
F. Ventura	2010	study design
F. Verhoeven	2018	off-topic
D. G. Vilas	2012	off-topic
G. D. Weinstein	1970	off-topic
V. C. Weiss	1985	off-topic
L. U. Wolfer	1996	off-topic
M. C. Wu and J. Y. Lee	2012	off-topic
T. Yamamoto	2005	no relevant outcomes
T. Yamamoto	2005	no relevant outcomes
S. Yanagihara	2017	double
S. Yanagihara	2017	study design
H. Zachariae	1984	off-topic
H. Zachariae	1988	off-topic
M. Zanni	2011	study design
M. Zarei	2016	double
N. N. Zein	2005	off-topic

References (EtD framework AND methods & evidence report)

1. Sbidian E, Chaimani A, Afach S, Doney L, Dressler C, Hua C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. The Cochrane database of systematic reviews. 2020;1:Cd011535.
2. Ighani A, Partridge ACR, Shear NH, Lynde C, Gulliver WP, Sibbald C, et al. Comparison of Management Guidelines for Moderate-to-Severe Plaque Psoriasis: A Review of Phototherapy, Systemic Therapies, and Biologic Agents. Journal of cutaneous medicine and surgery. 2018:1203475418814234.
3. Rencz F, Kemeny L, Gajdacsi JZ, Owczarek W, Arenberger P, Tiplica GS, et al. Use of biologics for psoriasis in Central and Eastern European countries. Journal of the European Academy of Dermatology and Venereology : JEADV. 2015;29(11):2222-30.
4. Kojanova M, Fialova J, Cetkovska P, Gkalpakiotis S, Jircikova J, Dolezal T, et al. Characteristics and risk profile of psoriasis patients included in the Czech national registry BIOREP and a comparison with other registries. International journal of dermatology. 2017;56(4):428-34.
5. Mrowietz U, Kragballe K, Reich K, Spuls P, Griffiths CE, Nast A, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Archives of dermatological research. 2011;303(1):1-10.
6. Llamas-Velasco M, de la Cueva P, Notario J, Martinez-Pilar L, Martorell A, Moreno-Ramirez D. Moderate Psoriasis: A Proposed Definition. Actas dermo-sifiliograficas. 2017;108(10):911-7.
7. Strober B, Ryan C, van de Kerkhof P, van der Walt J, Kimball AB, Barker J, et al. Recategorization of psoriasis severity: Delphi consensus from the International Psoriasis Council. Journal of the American Academy of Dermatology. 2020;82(1):117-22.
8. Mrowietz U, Barker J, Boehncke WH, Iversen L, Kirby B, Naldi L, et al. Clinical use of dimethyl fumarate in moderate-to-severe plaque-type psoriasis: a European expert consensus. Journal of the European Academy of Dermatology and Venereology : JEADV. 2018;32 Suppl 3:3-14.
9. Mahil SK, Wilson N, Dand N, Reynolds NJ, Griffiths CEM, Emsley R, et al. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study (the British Association of Dermatologists Biologics and Immunomodulators Register, BADBIR). British Journal of Dermatology.n/a(n/a).
10. Florek AG, Wang CJ, Armstrong AW. Treatment preferences and treatment satisfaction among psoriasis patients: a systematic review. Archives of dermatological research. 2018;310(4):271-319.
11. Schielein MC, Tizek L, Rotter M, Konstantinow A, Biedermann T, Zink A. Guideline-compliant prescription of biologicals and possible barriers in dermatological practices in Bavaria. Journal of the European Academy of Dermatology and Venereology : JEADV. 2018;32(6):978-84.
12. http://www.bad.org.uk/healthcare-professionals/clinical-standards/clinical-guidelines, accessed 19 February 2020,, .
13. Radtke MA, Reich K, Blome C, Kopp I, Rustenbach SJ, Schafer I, et al. Evaluation of quality of care and guideline-compliant treatment in psoriasis. Development of a new system of quality indicators. Dermatology (Basel, Switzerland). 2009;219(1):54-8.
14. Dressler C, Eisert L, Pham PA, Nast A. Efficacy and safety of systemic treatments in psoriatic arthritis: a systematic review, meta-analysis and GRADE evaluation. Journal of the European Academy of Dermatology and Venereology : JEADV. 2019;33(7):1249-60.
15. Pham PA, Dressler C, Eisert L, Nast A, Werner RN. Time until onset of action when treating psoriatic arthritis: meta-analysis and novel approach of generating confidence intervals. Rheumatology international. 2019;39(4):605-18.
16. Higgins JPT, Green S, Cochrane C. Cochrane handbook for systematic reviews of interventions [Oxford]: Cochrane Collaboration; 2011. Available from: http://www.cochrane-handbook.org/.
17. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011;64(4):383-94.

18. Al-Mutairi N, Shabaan D. Effects of tumor necrosis factor alpha inhibitors extend beyond psoriasis: insulin sensitivity in psoriasis patients with type 2 diabetes mellitus. Cutis. 2016;97(3):235-41.
19. Kimball AB, Bensimon AG, Guerin A, Yu AP, Wu EQ, Okun MM, et al. Efficacy and safety of adalimumab among patients with moderate to severe psoriasis with co-morbidities: Subanalysis of results from a randomized, double-blind, placebo-controlled, phase III trial. Am J Clin Dermatol. 2011;12(1):51-62.
20. Koenig AS, Szumski A, Pedersen R, Robertson DH. Impact of etanercept therapy on glycemic control in a cohort of psoriatic patients: The pristine trial

Arthritis and Rheumatism Conference: Annual Scientific Meeting of the American College of Rheumatology and Association of Rheumatology Health Professionals. 2011;63(10 SUPPL. 1).
21. Pinter A, Gerdes S, Papavassilis C, Reinhardt M. Characterization of responder groups to secukinumab treatment in moderate to severe plaque psoriasis. Journal of Dermatological Treatment. 2019.
22. Hong JR, Lee YW, Choe YB, Ahn KJ. Risk factors for increased serum creatinine level in patients with psoriasis treated with cyclosporine in a real-world practice. Dermatologic Therapy. 2019;32 (3) (no pagination)(e12875).
23. Kalb RE, Fiorentino DF, Lebwohl MG, Toole J, Poulin Y, Cohen AD, et al. Risk of Serious Infection With Biologic and Systemic Treatment of Psoriasis: Results From the Psoriasis Longitudinal Assessment and Registry (PSOLAR). JAMA Dermatol. 2015;151(9):961-9.
24. Wu JJ, Liu L, Asgari MM, Curtis JR, Harrold L, Salman C, et al. Initiation of TNF inhibitor therapy and change in physiologic measures in psoriasis. J Eur Acad Dermatol Venereol. 2014;28(10):1380-7.
25. Wu JJ, Rowan CG, Bebchuk JD, Anthony MS. No association between TNF inhibitor and methotrexate therapy versus methotrexate in changes in hemoglobin A1C and fasting glucose among psoriasis, psoriatic arthritis, and rheumatoid arthritis patients. J Drugs Dermatol. 2015;14(2):159-66.
26. OCEBM Levels of Evidence Working Group, * OCEBM Levels of Evidence Working Group = Jeremy Howick ICJLL, Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson. “The Oxford Levels of Evidence 2”2011 10 August 2018. Available from: https://www.cebm.net/2016/05/ocebm-levels-of-evidence/.
27. Higgins JPT SJ, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A ;. revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. Cochrane Database of Systematic Reviews. 2016.
28. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, et al. Secukinumab in plaque psoriasis--results of two phase 3 trials. The New England journal of medicine. 2014;371(4):326-38.
29. Blauvelt A, Reich K, Tsai TF, Tyring S, Vanaclocha F, Kingo K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: Results from the CLEAR study. J Am Acad Dermatol. 2017;76(1):60-9.e9.
30. Menter A, Tyring SK, Gordon K, Kimball AB, Leonardi CL, Langley RG, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. Journal of the American Academy of Dermatology. 2008;58(1):106-15.
31. Strohal R, Puig L, Chouela E, Tsai TF, Melin J, Freundlich B, et al. The efficacy and safety of etanercept when used with as-needed adjunctive topical therapy in a randomised, double-blind study in subjects with moderate-to-severe psoriasis (the PRISTINE trial). The Journal of dermatological treatment. 2013;24(3):169-78.

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