VIII. Methods Section

For the detailed description of the guideline development process, please see guideline report.

This report is available alongside the guideline document on the EDF website: https://www.guidelines.edf.one/ Details on the Update 2023 can be found below.

In short, the guideline development group is comprised of 24 dermatology experts from 14 countries, two patient representatives nominated by IFPA and the EuroGuiDerm methodologists. One patient representative participated actively in the 2023 update. The guideline draft texts and recommendations were developed by the experts in working groups, reviewed, discussed and amended where appropriate by the entire group. All votings were done with a minimal agreement of >50%. A structured consensus technique was used during the consensus conference.

Wording as suggested by the GRADE Working Group to standardize the wording of all recommendations was used [1], see below.

Wording of recommendations [2-5]

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

Weak recommendation **against** the use of an intervention	'We suggest against . . .'	↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
Strong recommendation **against** the use of an intervention	'We recommend against . . .'	↓↓	We believe that all or almost all informed people would make a choice against that intervention. This recommendation can be adopted as a policy in most clinical situations.

The recommendations are presented throughout this guideline as displayed below: first the content, then the arrows and colours indicating the direction and the strength of the recommendations, respectively and lastly the rate of expert agreement (consensus strength). Evidence-based recommendations are indicated as such.

We **recommend** to do tuberculosis screening according to local regulations.	↑↑	Strong consensus[1] 100 % Agreement Expert consensus

[1] due to personal-financial conflict of interest x abstentions

The tables 'instruction for use' and 'lab controls' have also been voted on – these are consensus-based. The rate of expert agreement is displayed too.

An internal & external review was conducted. Dissemination, implementation and monitoring plans were developed as well as a joint Q&A section for patients. For more details, see Methods & Evidence report.

Update 2023

In May 2022, an update of the Cochrane review has been published [6].

The EuroGuiDerm Team updated the three systematic reviews supporting the chapters on psoriatic arthritis, heart disease and diabetes. Author groups were provided with a summary of the results (details on the methods and results can be found online).

In March 2023, deucravacitinib has been licensed for the treatment of psoriasis vulgaris, consequently all authors reviewed their chapters. The following sections changed and were voted on:

- New chapter on deucravacitinib,
- Psoriatic arthritis

- Diabetes mellitus
- Viral hepatitis
- Depression
- Tuberculosis screening
- The algorithm as well as the decision grid.

The above mentioned changes were presented to the GDG in an online survey. All experts were asked to vote (agree / disagree/comment). Alternative suggestions could be entered as a reply option. Voting was not anonymous but experts could not see how others had voted. Only the EuroGuiDerm Team had access to the results. All authors could participate but the votes of those with personal financial conflicts of interest did not count.

Six of 25 experts (24%) declared personal-financial conflicts of interest (see below), meaning that they did not vote or their vote was not counted. One external expert declared personal-financial conflicts of interest and was not entitled to vote. Alexander Nast is the guideline coordinator and did not vote. He does not have any personal-financial conflicts of interests.

Title	First name	Last name	Personal- financial conflicts of interest
Prof.	Zsuzsanna	Bata-Csörgő	none
Prof.	Ivan	Bogdanov	none
Dr.	Hugo	Boonen	I have been asked for presentations concerning different products to treat psorias. But I don't get money for prescription of certain medication. I am also member of the Belgian Psoriasis working group who gives advice to all kinds of treatment options.
Prof.	Elke MGJ	de Jong	none
Dr.	Ignacio	Garcia-Doval	Reports payment from Novartis and UCB for presentations unrelated to psoriasis (on meta-analysis and critical reading); personal payment
Prof.	Paolo	Gisondi	I have received compensation (payments) for acting as a speaker for Abbvie, Novartis, UCB
Dr.	Diljit	Kaur-Knudsen	none
Prof.	Pietro	Lampertico	Advisory Board/Speaker Bureau for: - ROCHE PHARMA/DIAGNOSTICS, GILEAD SCIENCES, GSK, ABBVIE, JANSSEN, MYR, EIGER, ANTIOS, ALIGOS, VIR, GRIFOLS, ALTONA, ROBOSCREEN (external expert, not entitled to vote)
Dr.	Satveer	Mahil	none
Dr.	Tarja	Mälkönen	Consultancy fees (Abbvie, Janssen, Lilly, Novartis)
Prof.	Vincent	Mallet	none
Dr.	Julia-Tatjana	Maul	none
	Sicily	Mburu	none
Dr.	Liam	Mercieca	none
Prof.	Ulrich	Mrowietz	Honoraria as advisor and/or speaker: AbbVie, Aditxt, Almirall, Amgen, Aristea, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly, Immunic, Janssen-Cilag, LEO Pharma, Merck, Sharp & Dohme, Novartis, UCB Pharma, UNION therapeutics.

Title	First name	Last name	Personal- financial conflicts of interest
Prof.	Alexander	Nast	none
Prof.	Eva	Remenyik	none
Prof.	Dimitris	Rigopolous	none
Dr.	Kirsten Marthine	Rønholt Stausholm	*Has left the group*
Dr.	Paul-Gunther	Sator	none
Prof.	Marcus	Schmitt-Egenolf	none
Dr.	Mariusz	Sikora	none
Prof.	Catherine	Smith	none
Prof.	Phyllis I.	Spuls	none
Dr.	Olav	Sundnes	none
Dr.	Klaus	Strömer	none
	David	Trigos	*Has left the group*
	Gayle	van der Kraaij	none
Prof.	Nikhil	Yawalkar	Personal fees from Abbvie, Allmiral, Amgen, Celgene, Boehringer Ingelheim, Bristol Myers Squibb, Essex/MSD, Janssen, Leo, Lilly, Novartis, Pfizer, UCB
	Martin	Dittmann	none
Dr.	Maria	Kinberger	none
	Antonia	Pennitz	none
	Isabell	Vader	none
	Christoph	Zeyen	none

The EuroGuiDerm Living Psoriasis Guideline was updated and we disseminated this through various channels including social media and newsletters.

We would like to thank the following experts for their input on a specific chapter:

Viral hepatitis	The update of this chapter was developed together with Professor Pietro Lampertico, Milan, Itlay and Professor Vincent Mallet, Paris, France. Both were nominated by the European Association for the Study of the Liver (EASL)

Excerpt from the abstract of the Cochrane Review 'Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis (Review) ' by Emilie Sbidian and colleagues, May 2022.

"[...] Network meta-analysis at class level showed that all interventions (non-biological systemic agents, small molecules, and biological treatments) showed a higher proportion of patients reaching PASI 90 than placebo. Anti-IL17 treatment showed a higher proportion of patients reaching PASI 90 compared to all the interventions, except anti-IL23. Biologic treatments anti-IL17, anti-IL12/23, anti-IL23 and anti-TNF alpha showed a higher proportion of patients reaching PASI 90 than the non-biological systemic agents.

For reaching PASI 90, the most effective drugs when compared to placebo were (SUCRA rank order, all high-certainty evidence): infliximab (risk ratio (RR) 50.19, 95% CI 20.92 to 120.45), bimekizumab (RR 30.27, 95% CI 25.45 to 36.01), ixekizumab (RR 30.19, 95% CI 25.38 to 35.93), risankizumab (RR 28.75, 95% CI 24.03 to 34.39). Clinical effectiveness of these drugs was similar

when compared against each other. Bimekizumab, ixekizumab and risankizumab showed a higher proportion of patients reaching PASI 90 than other anti-IL17 drugs (secukinumab and brodalumab) and guselkumab. Infliximab, anti-IL17 drugs (bimekizumab, ixekizumab, secukinumab and brodalumab) and anti-IL23 drugs (risankizumab and guselkumab) except tildrakizumab showed a higher proportion of patients reaching PASI 90 than ustekinumab and three anti-TNF alpha agents (adalimumab, certolizumab and etanercept). Ustekinumab was superior to certolizumab; adalimumab and ustekinumab were superior to etanercept. No significant difference was shown between apremilast and two non-biological drugs: ciclosporin and methotrexate.

We found no significant difference between any of the interventions and the placebo for the risk of SAEs. The risk of SAEs was significantly lower for participants on methotrexate compared with most of the interventions. Nevertheless, the SAE analyses were based on a very low number of events with low- to moderate-certainty for all the comparisons (except methotrexate versus placebo, which was high-certainty). The findings therefore have to be viewed with caution.

For other efficacy outcomes (PASI 75 and Physician Global Assessment (PGA) 0/1), the results were similar to the results for PASI 90. Information on quality of life was often poorly reported and was absent for several of the interventions. […] ". page 6, Sbidian et al. 2022 [6]

EUROGUIDERM GUIDELINE FOR THE TREATMENT OF PSORIASIS VULGARIS. SYSTEMIC TREATMENT	EUROPEAN CENTRE FOR GUIDELINES DEVELOPMENT  European Dermatology Forum CHARITÉ d:EBM

Plaque type psoriasis: Evidence to decision framework, Update 2023

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) or tyrosinekinase inhibitor (deuravacitinib) 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	TYK-2 inhibitors
Acitretin	Apremilast	Adalimumab	Ustekinumab	Brodalumab	Guselkumab	Deucravacitinib
Ciclosporin		Certolizumab		Bimekizumab	Rizankizumab	
FAEs		Etanercept		Ixekizumab	Tildrakizumab	
Methotrexate		Infliximab		Secukinumab		

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)

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) or tyrosinekinase inhibitor (deuravacitinib) compared with each other or with placebo?	
	Evidence synthesis in cooperation with: Cochrane Review 'Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis (Review) ' by Emilie Sbidian and colleagues, May 2022 [6]
CONFLICT OF INTERESTS:	Less than 50% of the guideline development committee declared to have personal-financial conflicts of interests (see Methods Report of this guideline).

Linking evidence to recommendations

Recommendation 2023
We **recommend** to take efficacy and safety (see Cochrane Review and drug chapters), time until onset of treatment response, comorbidities (see decision grids, section Guidance for specific clinical and comorbid situations), and individual patient factors into account when choosing a systemic treatment for moderate or severe psoriasis. In addition, national regulations and reimbursement circumstances need to be taken into consideration and treatment algorithms should be developed on a national level.
We **recommend** the initiation of systemic treatment in patients with moderate to severe psoriasis* (as defined in each country, see also section "Defining disease severity"). **UV therapy is not part of this guideline but it is recommended as an alternative induction therapy if suitable.*
For most patients who require systemic treatment, we recommend choosing a treatment from the group of the 'conventional systemic agents'.
For cases of severe disease, we suggest following Figure 1 in long version.
In cases of inadequate response, contra-indication or intolerability we recommend following Figure 1 in long version.
League table below: Short term (8-24 weeks), RR and 95% CI; RRs larger than 1 for the lower triangle and smaller than 1 for the upper triangle favour the treatment on the left. Certainty of evidence high (highlighted in green), moderate (in blue), low (in yellow) and very low (in red). Source: Sbidian et al. 2022   Cochrane Review 'Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis (Review) ' by Emilie Sbidian and colleagues, May 2022, Figure 7[6]

Serious adverse events

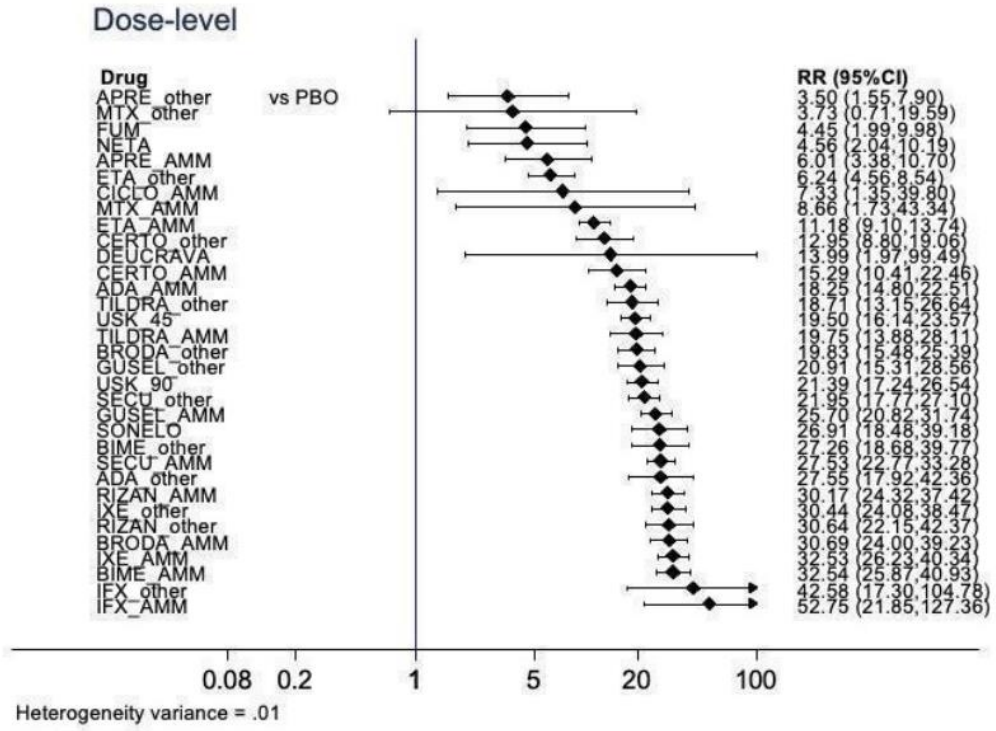
Number of participants (studies)	1693 (6)	1730 (4)	5775 (7)	2930 (8)	8459 (20)	313 (1)	4579 (5)	4467 (7)	11342 (16)	2217 (3)	267 (1)	5440 (11)	1323 (5)	8464 (14)	127 (1)	120 (1)	2676 (7)	213 (1)	1130 (2)	-	
1693 (6)	IFX	2.26 (0.81,6.33)	1.30 (0.57,2.97)	1.62 (0.69,3.76)	1.11 (0.50,2.45)	0.95 (0.16,5.50)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

PASI 90

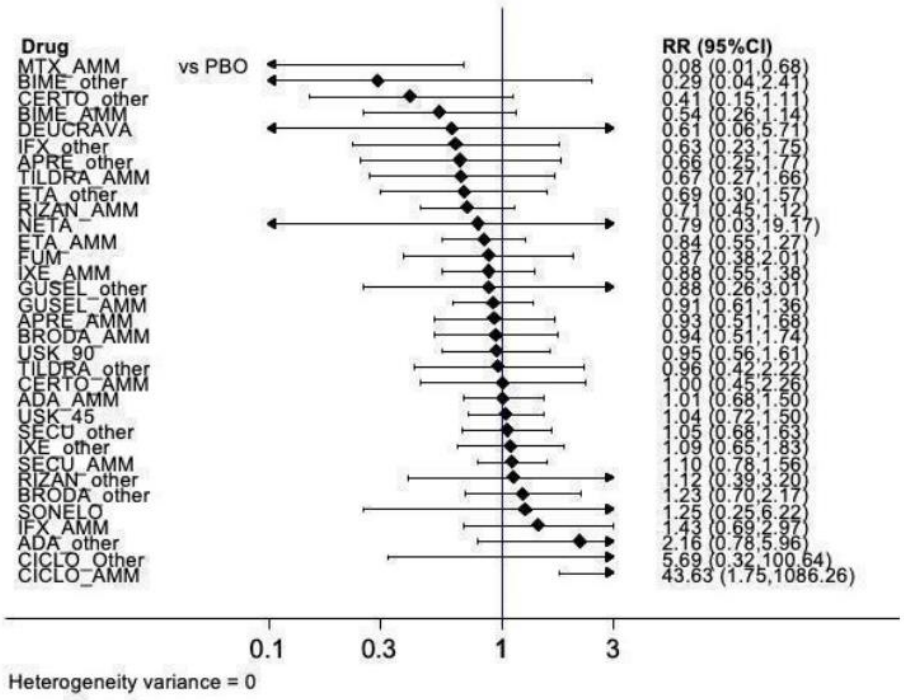
Justification
All treatment options were found to be efficacious when compared to placebo. Recommendations were drafted along the line of drug licensing, taking practical aspect of reimbursement into account. National societies may develop different recommendations reflecting the national reimbursement situation. Following the label, for most patients a 'conventional' is considered as the first treatment option. Taking into consideration the higher efficacy of approved European Medical Agency (EMA) first label biologics, a "first line use" of biologics is considered in patients with severe psoriasis. For the selection of a treatment among the 'conventionals', first line biologics and biologics / small molecules in general, many different factors need to be taken into account (see also "specific treatment circumstances") and no clear hierarchy has been decided upon by the guideline group.

"Relative effects of the intervention as estimated from the network meta-analysis model for Psoriasis Area and Severity Index (PASI) 90 and serious adverse events (SAEs) Outcomes were all measured at the induction phase (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) of the intervention in the respective column versus the comparator in the respective row. RRs larger than 1 for the lower triangle and smaller than 1 for the upper triangle favour the treatment on the left. Certainty of evidence was assessed for each comparison using CINeMA and classified in high (highlighted in green), moderate (in blue), low (in yellow) and very-low (in red). Significant results are highlighted in bold. ACI: acitretin; ADA: adalimumab; APRE: apremilast; BIME: bimekizumab; BRODA: brodalumab; CERTO: certolizumab; CICLO: ciclosporin; DEUCRAVA: deucravacitinib; ETA: etanercept; FUM: fumaric acid; IFX: infliximab; IXE: ixekizumab; GUSEL: guselkumab; MTX: methotrexate; NETA: netakimab; PBO: placebo; RISAN: risankizumab; SECU: secukinumab; SONELO: sonelokimab; TILDRA: tildrakizumab; USK: ustekinumab" [6]

Sensitivity analysis for approved dosages versus other dosages



PASI 90



Serious adverse events

"Sensitivity analyses - Interval plot. Network meta-analysis results for primary outcomes (PASI 90 and serious adverse events, left and right forest plot respectively) for all the interventions depending on the doses: approved dosages versus other dosages Outcomes were measured at the induction phase (assessment from 8 to 24 weeks after randomisation). MTX_AMM/Other: methotrexate ≥ 15 mg per week/ < 15 mg per week; CICLO_AMM/ Other: ciclosporin ≥ 3 mg/kg/day/<3 mg/kg/day; ACI_AMM/Other: acitretin ≥ 35 mg per day/<35 mg per day; FUM: fumaric acid esters all dosages; APRE_AMM/Other: apremilast 30 mg twice daily/other dosages; ETA_AMM/Other: etanercept 50 mg twice a week/Other dosage; IFX_AMM/Other: infliximab 5 mg/kg

week 0, 2, 4 every 6 weeks/Other dosages; ADA_AMM/Other: adalimumab 80 mg Week 0, 40 mg Week 1 then 40 mg every other week/Other dosages; CERTO_AMM/Other: certolizumab 400 mg at week 0,2,4 then 400 mg every other week or other dosages/Other dosages; USK 45/90: ustekinumab 45/90 mg; SECU_AMM/Other: secukinumab 300 mg at week 0, 1, 2, 3, and 4 then every 4 weeks or other dosages/other dosages; IXE_AMM/Other: ixekizumab 160 mg at Week then 80 mg every other weeks until week 12 then 80 mg monthly or other dosages; TILDRA_AMM/Other: tildrakizumab 100 mg at week 0 and 4 then every 12 weeks/Other dosages; GUSEL 100: guselkumab 100 mg per injection; BRODA_AMM/Other: brodalumab 210 mg at week 0, 1, 2 then every other weeks/other dosages; RISAN_AMM/Other: risankizumab, S/C, 150 mg (two 75 mg injections) at Week 0, Week 4 and every 12 weeks thereaſter/other dosages; BIME_AMM/Other: bimekizumab, S/C, 320 mg (2 x 160 mg injections) at week 0, 4, 8, 12, 16 and every 8 weeks thereaſter/other dosages. DEUCRACA (deucravacitinib), SONELO (sonelokimab) and NETA (netakimab) were grouped in one dosage whatever the dosages. CI: confidence interval; PASI: Psoriasis Area and Severity Index; RR: risk ratio; AMM: 'approved dosage'" [6]

Relative effects of the class-level intervention as estimated from the network meta-analysis model

SAE

AIL17	1.19 (0.91,1.54)	0.96 (0.70,1.33)	1.04 (0.78,1.38)	1.12 (0.63,2.01)	1.28 (0.58,2.81)	0.95 (0.76,1.20)
1.14 (0.95,1.36)	AIL23	0.81 (0.57,1.16)	0.87 (0.64,1.19)	0.94 (0.52,1.72)	1.08 (0.48,2.40)	0.80 (0.61,1.06)
1.45 (1.23,1.71)	1.27 (1.04,1.56)	AIL1223	1.07 (0.74,1.57)	1.16 (0.62,2.18)	1.33 (0.59,3.02)	0.99 (0.71,1.38)
1.95 (1.64,2.33)	1.72 (1.44,2.05)	1.35 (1.10,1.66)	ATA	1.08 (0.61,1.94)	1.24 (0.56,2.73)	0.92 (0.71,1.19)
2.96 (1.63,5.38)	2.60 (1.42,4.74)	2.04 (1.11,3.74)	1.51 (0.84,2.72)	SM	1.14 (0.45,2.88)	0.85 (0.50,1.45)
5.74 (2.40,13.73)	5.04 (2.10,12.13)	3.95 (1.64,9.53)	2.93 (1.22,7.03)	1.94 (0.69,5.45)	CSA	0.74 (0.35,1.57)
26.78 (22.07,32.49)	23.53 (19.00,29.15)	18.47 (14.82,23.02)	13.70 (11.22,16.73)	9.06 (5.06,16.23)	4.67 (1.99,10.94)	PBO

PASI90

Adverse events

AIL17	1.12 (1.05,1.19)	1.06 (1.00,1.12)	1.06 (1.01,1.12)	0.91 (0.82,1.01)	0.99 (0.86,1.15)	1.14 (1.09,1.19)
1.08 (0.97,1.20)	AIL23	0.94 (0.88,1.02)	0.95 (0.89,1.01)	0.81 (0.72,0.90)	0.89 (0.76,1.03)	1.02 (0.96,1.08)
1.18 (1.08,1.29)	1.09 (0.98,1.22)	AIL1223	1.00 (0.94,1.07)	0.86 (0.77,0.96)	0.94 (0.80,1.09)	1.08 (1.02,1.14)
1.47 (1.33,1.62)	1.36 (1.23,1.51)	1.24 (1.11,1.39)	ATA	0.85 (0.77,0.95)	0.94 (0.80,1.09)	1.07 (1.03,1.12)
2.67 (2.04,3.51)	2.48 (1.89,3.27)	2.27 (1.72,2.99)	1.82 (1.40,2.38)	SM	1.10 (0.92,1.30)	1.26 (1.15,1.39)
5.22 (3.72,7.32)	4.85 (3.44,6.83)	4.43 (3.15,6.23)	3.56 (2.54,4.99)	1.95 (1.29,2.94)	CSA	1.15 (1.00,1.33)
13.43 (12.00,15.03)	12.48 (11.03,14.11)	11.39 (10.08,12.88)	9.15 (8.20,10.21)	5.02 (3.89,6.48)	2.57 (1.87,3.54)	PBO

PASI75

Quality of life

AIL17	0.04 (-0.28,0.35)	-0.04 (-0.39,0.31)	-0.29 (-0.54,-0.03)	-0.94 (-1.32,-0.56)	-0.32 (-1.17,0.53)	-1.37 (-1.60,-1.14)
1.19 (1.01,1.41)	AIL23	-0.07 (-0.39,0.24)	-0.32 (-0.57,-0.07)	-0.97 (-1.35,-0.60)	-0.35 (-1.20,0.49)	-1.41 (-1.63,-1.18)
1.36 (1.17,1.60)	1.14 (0.95,1.37)	AIL1223	-0.25 (-0.54,0.05)	-0.90 (-1.29,-0.50)	-0.28 (-1.13,0.58)	-1.33 (-1.59,-1.07)
1.69 (1.44,1.99)	1.42 (1.21,1.67)	1.24 (1.03,1.49)	ATA	-0.65 (-0.98,-0.32)	-0.03 (-0.86,0.80)	-1.08 (-1.23,-0.94)
3.58 (2.54,5.03)	3.00 (2.12,4.23)	2.62 (1.85,3.72)	2.11 (1.51,2.94)	SM	0.62 (-0.25,1.49)	-0.43 (-0.73,-0.14)
5.56 (3.56,8.68)	4.66 (2.97,7.32)	4.08 (2.59,6.41)	3.28 (2.10,5.12)	1.55 (0.92,2.62)	CSA	-1.05 (-1.87,-0.24)
14.41 (12.32,16.85)	12.07 (10.22,14.25)	10.56 (8.90,12.54)	8.50 (7.31,9.88)	4.03 (2.95,5.49)	2.59 (1.70,3.95)	PBO

PGA

"Outcomes were all measured at the induction phase (assessment from 8 to 24 weeks after randomisation). Drugs are reported in order of primary benefit ranking. Each cell contains the risk ratio (RR) (for dichotomous outcomes: PASI 90, serious adverse events, PASI 75, PGA 0/1, adverse events) or the standardised mean difference (SMD) (for the quality-of-life outcome), plus the 95% confidence interval, of the class level in the respective column versus the class level in the respective row. RRs larger than 1 for the lower triangle and smaller than 1 (or SMDs smaller than zero) for the upper triangle favour the treatment on the left. Significant results are highlighted in grey. AE: adverse events; PASI: Psoriasis Area and Severity Index; PGA: Physician's Global Assessment; QoL: quality of life; SAE: serious adverse events; SAE without worsening of psoriasis correspond to SAE after exclusion of flares of psoriasis; AIL12/23: anti-IL12/23; AIL17: anti-IL17; AIL23: anti-IL23, ATA: anti-TNF alpha; CSA: non-biological conventional systemic agents; PBO: placebo; SM: small molecules" [6]

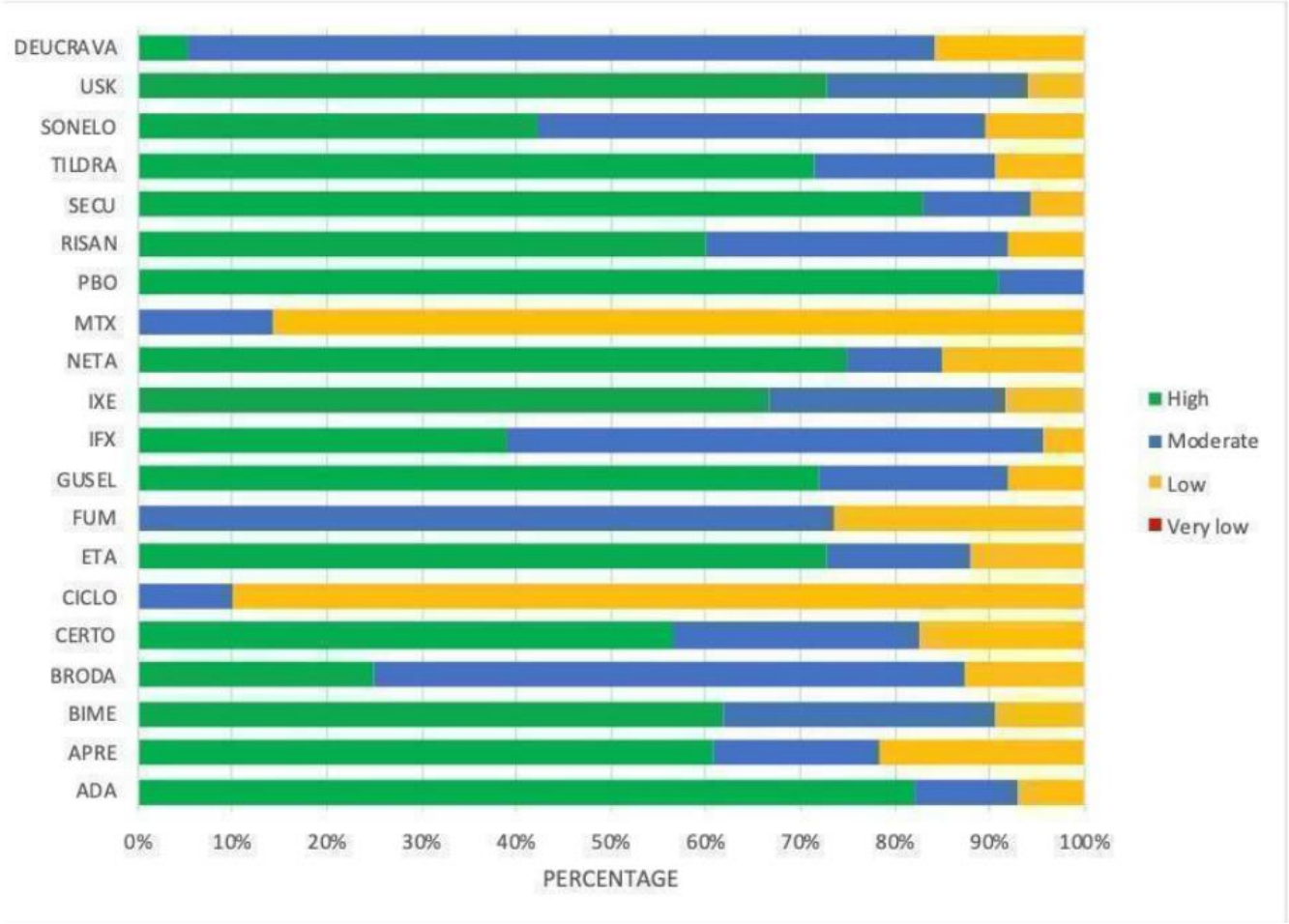
Certainty of evidence

What is the overall certainty of the evidence of effects?

Note that CINeMA not GRADE was used. [7,8]

PASI 90

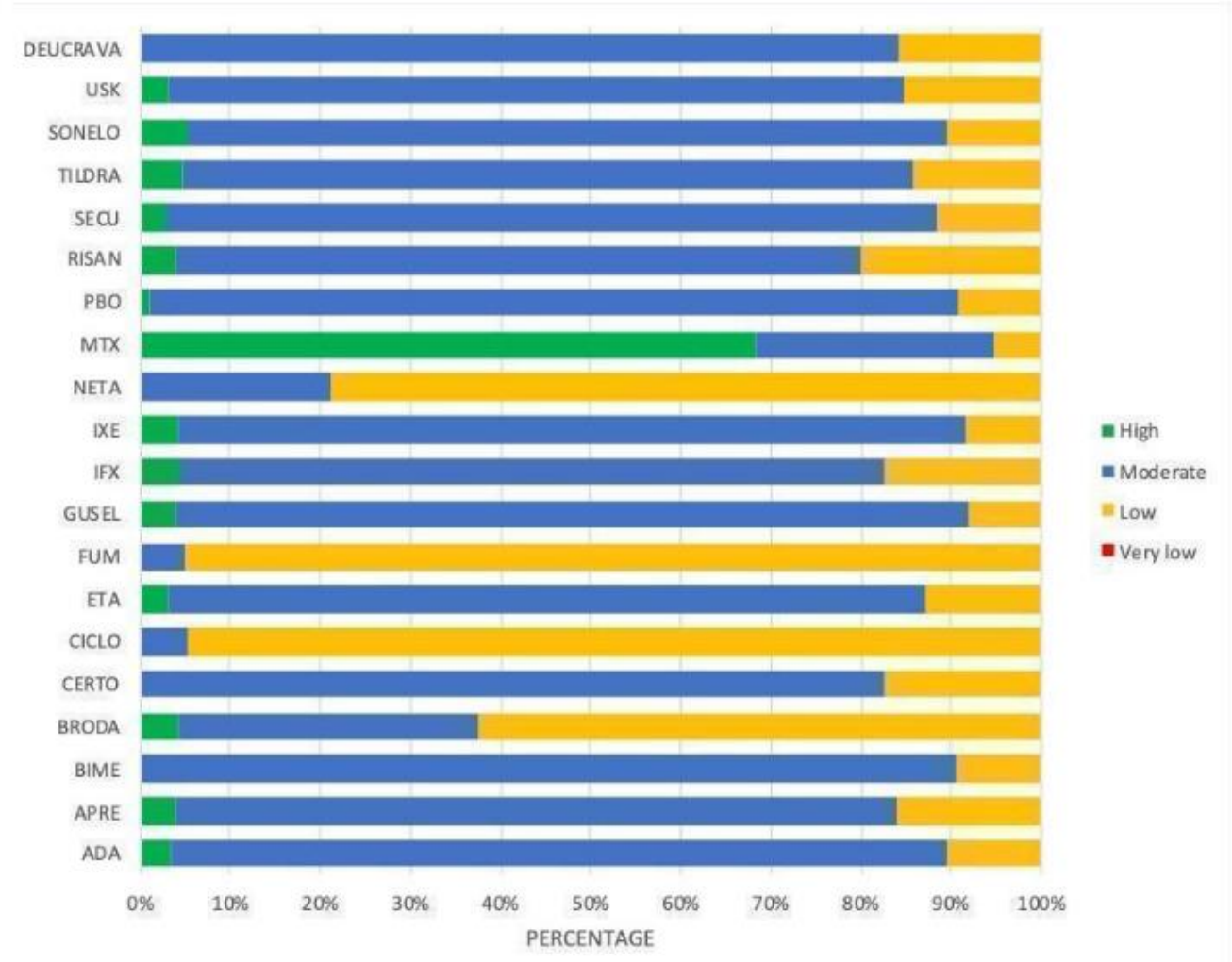
"Certainty of evidence per drug for PASI 90 using CINeMA Each drug is presented as a bar, which indicates the composition of the 4-level confidence of evidence from all comparisons including that drug. Green: high confidence; blue: moderate confidence; yellow: low confidence; red: very low confidence. ACI: acitretin; ADA: adalimumab; APRE: apremilast; BIME: bimekizumab; BRODA: brodalumab; CERTO: certolizumab; CICLO: ciclosporin; CINeMA: Confidence in Network Meta-Analysis; DEUCRAVA: deucravacitinib; ETA: etanercept; FUM: fumaric acid; IFX: infliximab; IXE: ixekizumab; GUSEL: guselkumab; MTX: methotrexate; NETA: netakimab; PASI: Psoriasis Area and Severity Index; PBO: placebo; RISAN: risankizumab; SECU: secukinumab; SONELO: sonelokimab; TILDRA: tildrakizumab; USK: ustekinumab" [6]



Serious adverse events

"Certainty of evidence per drug for Serious Adverse Events using CINeMA Each drug is presented as a bar, which indicates the composition of the 4-level confidence of evidence from all comparisons including that drug. Green: high confidence; blue: moderate confidence; yellow: low confidence; red: very low confidence. ACI: acitretin; ADA: adalimumab; APRE: apremilast; BIME: bimekizumab; BRODA: brodalumab; CERTO: certolizumab; CICLO: ciclosporin; CINeMA: Confidence in Network Meta-Analysis; DEUCRAVA: deucravacitinib; ETA: etanercept; FUM: fumaric acid; IFX: infliximab; IXE: ixekizumab; GUSEL: guselkumab; MTX: methotrexate; NETA: netakimab; PBO:

placebo; RISAN: risankizumab; SECU: secukinumab; SONELO: sonelokimab; TILDRA: tildrakizumab; USK: ustekinumab" [6]



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