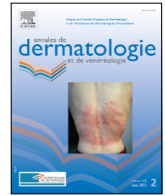




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Original article

# Treatment of moderate-to-severe psoriasis in adults: An expert consensus statement using a Delphi method to produce a decision-making algorithm



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## ABSTRACT

**Background:** New highly effective drugs for moderate-to-severe cutaneous psoriasis are regularly marketed, and the hierarchy of treatments thus requires frequent review.

**Objectives:** A Delphi method was used to enable a structured expert consensus on the use of systemic treatments and phototherapy among adults with moderate-to-severe psoriasis.

**Methods:** The Delphi method consists in achieving a convergence of opinions among a panel of experts using several rounds of questionnaires with controlled feedback between rounds. A two-part Delphi questionnaire was administered online to French psoriasis experts. In the first part, 180 items related to the prescription of systemic treatments and phototherapy for adult patients with moderate-to-severe psoriasis were grouped into 21 sections covering different lines of treatment and different forms of cutaneous psoriasis. The experts voted on each proposal using an ordinal 7-point Likert scale. The second part comprised 11 open-ended questions about special indications for each therapeutic class. These were converted into 101 questions for subsequent rounds. Consensus was deemed to have been reached if more than 80% of the experts agreed with a given proposal.

**Results:** Three rounds of questionnaires were sequentially sent to 35 participants between November 2021 and March 2022. Thirty-three (94%) completed all three rounds. For plaque psoriasis, only methotrexate was recommended by the experts as first-line systemic treatment (89% of votes). Cyclosporin was advocated in pustular and erythrodermic psoriasis, and acitretin was suggested for hyperkeratotic and palmoplantar psoriasis. In the event of failure of or intolerance to non-biological systemic treatments, guselkumab, risankizumab, ixekizumab or secukinumab were recommended by more than 80% of the experts. Tumor Necrosis Factor (TNF) inhibitors remain useful for patients with cardiovascular risk factors. Special indications were provided for each therapeutic class (methotrexate/narrow-band ultraviolet B phototherapy, psoralen/ultraviolet A phototherapy, cyclosporin, acitretin, apremilast, TNF inhibitors, interleukin (IL)-12/23 inhibitors, IL-17(R)A inhibitors, and IL-23 inhibitors).

**Conclusions:** This expert consensus statement indicates that newly available IL-17 and IL-23 inhibitors may be favored over TNF and IL-12/23 inhibitors as first-line biologics. The Centre of Evidence of the French Society of Dermatology has drawn up a decision-making algorithm to guide clinicians in the therapeutic management of moderate-to-severe psoriasis.

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## 1. Introduction

Psoriasis is a chronic inflammatory disease affecting the skin, the joints, or both. Its lifetime prevalence ranges from 1% to 5% worldwide [1]. Mild cutaneous psoriasis is usually managed with topical agents, while moderate-to-severe disease may require phototherapy or systemic therapy. Moderate-to-severe disease is typically defined as the involvement of more than 5 to 10 percent of the body surface area (BSA). Psoriasis can be severe irrespective of BSA where it significantly impacts physical, social or psychological well-being, or where it occurs in particular areas, including the palms, soles, face or genitalia [2–5]. Options for systemic therapy include immunosuppressive or immunomodulatory drugs such as methotrexate, cyclosporin, systemic retinoids, apremilast and biologic agents. As new drugs continue to be marketed, therapeutic guidelines require regular updating.

The French guidelines on the use of systemic treatments were released in 2019 and were based on the previous guidelines (the ADAPTE method) and a systematic review of the literature up to July 2017 [3]. Since the publication of these guidelines, the interleukin (IL)-23 inhibitors guselkumab, risankizumab and tildrakizumab, and the IL-17 inhibitor brodalumab have been marketed, and more than 55 randomized controlled trials (RCTs) have been conducted to evaluate the efficacy of these treatments [6].

Consequently, the Centre of Evidence of the French Society of Dermatology aimed to follow up on the 2019 French guidelines for the use of systemic treatments and phototherapy in moderate-to-severe psoriasis, and to construct a decision-making algorithm incorporating these recently-marketed drugs.

## 2. Materials and methods

### 2.1. The Delphi method

The Delphi method is a well-established tool for preparing guidelines based on expert consensus [7]. In brief, the goal of the Delphi method is to achieve a convergence of opinions among a panel of experts based on real-world knowledge of certain topics [8]. During the Delphi process, several rounds of questionnaires are submitted to a panel of experts. Controlled feedback is provided between the rounds, enabling the experts to reassess their answers in the light of the answers from other experts. The Delphi participants thus receive the questionnaire with a summary of the answers from the previous round, and they are able to modify their own answer [9,10].

### 2.2. Questionnaire

In March 2021, a working group comprising members of the Psoriasis Research group and the Centre of Evidence of the French Society of Dermatology (<https://centredepreuves.sfdermato.org/>) (FP, SL, GC, MC, FC, LG, NJ, LF) was formed to list (1) all systemic therapies available in France (non-biological systemic treatments, biologics and apremilast), (2) the rules to be used for the Delphi questionnaire (number of rounds, percentage of votes defining a consensus, number of points to be used on the Likert scale, etc.), and (3) the questions to be included in the questionnaire. After three meetings, the members agreed on a two-part questionnaire. In the first part, 180 questions grouped into 21 sections were to be

answered using a 7-point ordinal Likert scale rated from 1 (strongly disagree) to 7 (strongly agree). These related to first-line and second-line treatments for moderate-to-severe plaque psoriasis and to first-line treatments for specific forms of psoriasis. It was agreed to focus on first-line treatments for specific forms of psoriasis so as not to overload the questionnaire. In the second part, 11 open-ended questions were asked in the first round. These were converted into 101 yes/no questions or 7-point Likert scales for rounds 2 and 3. For statements with responses on an ordinal 7-point Likert scale, 'agreement' was defined as a score of 6–7, 'neutral' as a score of 3–5, and 'disagreement' as a score of 1–2. Consensus was deemed to have been reached where > 80% of the experts voted for a given option (agreement or disagreement). For binary questions, consensus was reached where > 80% experts voted for a particular option ('yes' or 'no'). If a consensus was reached, the question did not reappear in subsequent rounds. A total of three rounds was planned and completed. The members of the steering committee (FP, SL, LF) reviewed and interpreted the data from each round and implemented subsequent rounds based on the results from the previous round. During rounds 2 and 3, the participants were able to view the distribution of the experts' votes for each question in the previous round. All Delphi questions were to be answered. Reminder emails were sent to increase the response rate. No consensus meeting was planned. The Delphi study was conducted in accordance with the Guidance on Conducting and REporting DELphi Studies (CREDES) [11] and was registered on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT05144165).

### 2.3. Recruitment of participants

In September 2021, the members of the Centre of Evidence of the French Society of Dermatology met to define a list of 48 French physicians, all of whom were required to be dermatologists (in public or private practice, and active in different areas throughout France), members of the French Society of Dermatology, and actively involved in the management of patients with psoriasis and in psoriasis research, but excluding those participating in the design of the present study. It was decided to include the members of the scientific advisory board of the Psoriasis Research Group (GRPso) of the French Society of Dermatology and the members of the ResoPso board (a nationwide association of dermatologists particularly involved in the field of psoriasis). Once they had agreed to participate, the experts were sent an email containing a link to a web-based Welphi® survey. Before the first round, demographic information and details of any conflicts of interests were collected. All experts provided informed consent and reported any potential conflicts of interest.

## 3. Results

### 3.1. Participant characteristics

Of 48 experts contacted, 35 (72.9%) agreed to participate. Thirty-three (94.3%) completed all three rounds of the Delphi process (Table 1).

### 3.2. The Delphi process

Three web-based questionnaire rounds were conducted over a 5-month period. Rounds 1, 2 and 3 were conducted on November 9, 2021, January 11, 2022, and March 10, 2022, respectively (Fig. S1, supplementary material available online).

**Table 1**  
Demographic characteristics of the experts.

Characteristics	Experts (N = 33)
Age, years <sup>a</sup>	51.2 (10.5)
Female gender	22 (66.7)
Current position	
Public practice only (hospital)	20 (60.6)
Private practice only	2 (6.1)
Public and private practice	11 (33.3)
Number of patients treated for psoriasis (per month) <sup>a</sup>	
< 30	5 (15.2)
[30–60]	16 (48.5)
[60–90]	9 (27.2)
> 90	3 (9.1)
Phototherapy available	28 (84.8)

Data are expressed as means (standard deviation) for continuous data and as numbers (%) for categorical data.

<sup>a</sup> data missing for 1 expert.

### 3.3. Survey results

For patients with moderate-to-severe plaque psoriasis and without any contraindications (Table 2), consensus was reached from round 1 concerning the prescription of methotrexate (89% of the experts agreed). No consensus was reached for any other treatments. Narrowband ultraviolet (UV) B phototherapy was also frequently suggested by the experts but garnered only 69% of votes after three rounds. Cyclosporin, psoralen UVA phototherapy and apremilast were not recommended as first-line therapy for moderate-to-severe plaque psoriasis. In the event of failure of or intolerance to non-biological systemic treatments, guselkumab, risankizumab, ixekizumab and secukinumab were recommended by 91%, 85%, 83% and 82% of experts respectively (Table 3).

Methotrexate was the only first-line therapy recommended for palmoplantar psoriasis (91% of the experts agreed), nail psoriasis (85%), scalp psoriasis (85%), genital psoriasis (82%), seborrheic dermatitis (83%) and flexural psoriasis (82%). Cyclosporin was favored for pustular psoriasis (91%) and erythrodermic psoriasis (85%). Acitretin was frequently suggested as a first-line therapy for palmoplantar psoriasis and pustular psoriasis (67 and 73% respectively) (Table 4).

The experts highlighted the particular interest of specific first-line treatments in certain clinical situations (Table S1, supplementary material available online):

- (i) Methotrexate for patients with concomitant psoriatic arthritis (97% agreement).
- (ii) Cyclosporin where rapid action is required (88%), for pregnant patients, or for patients planning to have a child in the near future (94%).
- (iii) Narrowband UVB phototherapy as first-line treatment where heliotherapy/sun exposure is effective (88%), where the patient has a contraindication for systemic treatments (100%), is pregnant/plans to have a child in the near future (82%), or has an infectious comorbidity (including HIV or viral hepatitis) (85%).
- (iv) Acitretin for hyperkeratotic (97%) or palmoplantar psoriasis (88%), or for patients with active or recent cancer (85%). Acitretin may be combined with psoralen UVA phototherapy for hyperkeratotic psoriasis (82%).
- (v) Apremilast for patients with active or recent cancer (82%).

The experts highlighted the particular value of biologics in certain clinical situations:

- (i) Tumor Necrosis Factor (TNF) inhibitors for patients with cardiovascular risk factors (85%) or psoriatic arthritis (100%).

**Table 2**  
**Consensus and voting percentages by French psoriasis experts on first-line treatments for moderate-to-severe plaque psoriasis.** The experts were asked the following question: "In an adult patient with moderate-to-severe plaque psoriasis and no other comorbidities, previously treated with topical treatment only, and with no preference for or contraindications to a particular treatment (contraception in women), what do you usually prescribe as first-line therapy?"

Proposal	First round	Second round	Third round
Acitretin	12%	6%	3%
Cyclosporin	12%	6%	3%
<b>Methotrexate</b>	<b>89%</b>	–	–
Psoralen UVA phototherapy	26%	21%	12%
Acitretin + psoralen UVA phototherapy	15%	6%	–
Narrowband UVB phototherapy	63%	71%	69%
Apremilast (PDE-4 inhibitor)	12%	6%	–

Consensus regarding prescription is shown in bold.  
 – Where consensus was reached regarding the prescription or non-prescription of a given treatment, the question was not asked again in the subsequent round.

- (ii) IL-17 inhibitors for patients with concomitant psoriatic arthritis (97%) or where rapid action is required (100%).
- (iii) IL-23 inhibitors where rapid action is required (82%).

3.4. Consensus-based statement and decision-making algorithm

Using the Delphi results, the Centre of Evidence of the French Society of Dermatology drew up a decision-making algorithm based on the consensus statements obtained through the Delphi process. It was approved by the experts taking part in the survey (Fig. 1).

4. Discussion

The Delphi process generated a consensus among 33 French experts on 199 proposals involving systemic treatments or phototherapy for moderate-to-severe plaque psoriasis and for specific forms of psoriasis.

Methotrexate was favored as the first-line treatment among patients with moderate-to-severe plaque psoriasis without any contraindications. Narrowband UVB therapy is an acceptable choice, whereas it was concluded that psoralen UVA phototherapy or cyclosporin were no longer recommended for plaque psoriasis, possibly due to a less favorable benefit/risk ratio and to the greater constraints in daily life than with methotrexate or biologics. In the

case of failure of or intolerance to non-biological systemic treatments, IL-23 or IL-17 inhibitors were preferred over TNF or IL-12/23 inhibitors, which were recommended in the previous French guidelines [3]. Newly available biologics targeting IL-17 and IL-23 exhibit greater efficacy than TNF or IL-12/23 inhibitors in phase 3 RCTs regarding attainment of PASI 90 [6], which may explain why experts prioritize them today. For patients with cardiovascular risk factors (other than severe congestive heart failure), the experts favored TNF inhibitors, which may protect against cardiovascular events [12–14]. In addition, a higher risk of major adverse cardiovascular events was suggested in patients on IL-12/23 and IL-17 inhibitors, in contrast with TNF inhibitors [15,16].

The EuroGuiDerm guidelines were drawn up in 2020 by the European Dermatology Forum [17]. Acitretin, cyclosporin and fumarates (not available in France) were recommended, together with methotrexate as the first-line systemic treatment of choice. The TNF inhibitors adalimumab and certolizumab were recommended, together with IL-17 and IL-23 inhibitors, as a first choice for biologics. The guidelines issued by the British Association of Dermatologists and by the American Academy of Dermatology and National Psoriasis Foundation guidelines recommend any of the currently licensed biologic therapies [18–20]. These bodies chose not to provide any guidance in the selection of biologics.

For the present update, a Delphi approach was preferred to a systematic review for several reasons. While guidelines have often been drawn up using systematic reviews or meta-analyses of RCTs [3,17], these consist of head-to-head comparisons and primarily capture short-term efficacy and safety, whereas treatment selection is a multidimensional choice. Selection of treatment requires consideration of the following: rare or long-term adverse events (which are not well reported in RCTs), safety (adverse events can negatively impact daily life, even if they are not in themselves serious), and other parameters affecting clinician or patient preferences, such as the frequency of injections, clinical and laboratory monitoring, and treatment costs [21]. In our study, certain effective biologics were not prioritized by the experts, possibly due in part to the absence of an auto-injector/pen (brodalumab, tildrakizumab) or because of a higher frequency of injections (brodalumab). Thus, the Delphi method enables the adoption of a holistic approach based on the combination of evidence from the literature and expert opinion about various issues. The difficulty for the prescriber is the switch from population-level data to individual-level data. In 1996, Sackett *et al.* remarked that 'the practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence

**Table 3**  
**Consensus and voting percentages of French psoriasis experts on treatment of moderate-to-severe plaque psoriasis in case of failure of or intolerance to non-biological systemic treatments.** The experts were asked the following question: "In an adult patient with moderate-to-severe plaque psoriasis and no other comorbidities, previously treated with topical treatment only, and with no preference for or contraindications to a particular treatment (contraception in women), what do you usually prescribe in the event of failure of or intolerance to non-biological systemic treatments?"

Proposal		First round	Second round	Third round
TNF inhibitor	Adalimumab	25%	24%	18%
	Etanercept	0%	0%	–
	Infliximab	0%	0%	0%
	Certolizumab	12%	9%	6%
	Ustekinumab	48%	50%	63%
IL-12/23 inhibitor	<b>Guselkumab</b>	<b>75%</b>	<b>91%</b>	–
	Tildrakizumab	57%	71%	76%
	<b>Risankizumab</b>	<b>66%</b>	<b>80%</b>	<b>85%</b>
IL-17 inhibitor	<b>Secukinumab</b>	<b>69%</b>	<b>77%</b>	<b>82%</b>
	<b>Ixekizumab</b>	<b>72%</b>	<b>83%</b>	–
	Brodalumab	51%	62%	67%
	Apremilast	6%	–	–

Consensus regarding prescription is shown in bold.  
 – Where consensus was reached regarding the prescription or non-prescription of a given treatment, the question was not asked again in the subsequent round.  
 Bimekizumab was not included in the study because it was not available in France when the study was started.

**Table 4**  
**Consensus and voting percentages by French psoriasis experts on first-line treatments for specific forms of moderate-to-severe psoriasis.** The experts were asked the following question: "In an adult patient with moderate-to-severe [specific form of psoriasis] and no other comorbidities, previously treated with topical treatment only, with no preference for or contraindications to a particular treatment (contraception in women), what do you usually prescribe as first-line treatment?".

	Treatment	First round	Second round	Third round
<b>Palmoplantar psoriasis</b>	Acitretin	43%	56%	67%
	Cyclosporin	17%	9%	9%
	<b>Methotrexate</b>	<b>80%</b>	<b>91%</b>	–
	Psoralen UVA phototherapy	20%	24%	24%
	Acitretin + psoralen UVA phototherapy	15%	18%	18%
	Narrowband UVB phototherapy	3%	0%	–
	Apremilast (PDE-4 inhibitor)	0%	3%	–
<b>Pustular psoriasis</b>	Acitretin	44%	68%	73%
	<b>Cyclosporin</b>	<b>69%</b>	<b>77%</b>	<b>91%</b>
	Methotrexate	29%	33%	27%
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	3%	–	–
	Narrowband UVB phototherapy	6%	–	–
	Apremilast (PDE-4 inhibitor)	0%	–	–
<b>Erythrodermic psoriasis</b>	Acitretin	15%	6%	6%–
	<b>Cyclosporin</b>	<b>54%</b>	<b>74%</b>	<b>85%</b>
	Methotrexate	49%	59%	73%
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	0%	–	–
	Narrowband UVB phototherapy	9%	–	–
	Apremilast (PDE-4 inhibitor)	0%	–	–
<b>Nail psoriasis</b>	Acitretin	14%	6%	0%
	Cyclosporin	26%	27%	30%
	<b>Methotrexate</b>	<b>71%</b>	<b>85%</b>	–
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	0%	–	–
	Narrowband UVB phototherapy	0%	–	–
	Apremilast (PDE-4 inhibitor)	0%	0%	0%
<b>Genital psoriasis</b>	Acitretin	3%	3%	–
	Cyclosporin	25%	18%	15%
	<b>Methotrexate</b>	<b>72%</b>	<b>82%</b>	–
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	0%	–	–
	Narrowband UVB phototherapy	0%	–	–
	Apremilast (PDE-4 inhibitor)	9%	9%	9%
<b>Scalp psoriasis</b>	Acitretin	15%	6%	6%
	Cyclosporin	14%	6%	6%
	<b>Methotrexate</b>	<b>80%</b>	<b>85%</b>	–
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	0%	–	–
	Narrowband UVB phototherapy	0%	–	–
	Apremilast (PDE-4 inhibitor)	9%	9%	12%
<b>Sebopsoriasis</b>	Acitretin	3%	0%	–
	Cyclosporin	24%	12%	–
	<b>Methotrexate</b>	<b>83%</b>	–	–
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	0%	–	–
	Narrowband UVB phototherapy	0%	–	–
	Apremilast (PDE-4 inhibitor)	9%	6%	3%
<b>Flexural psoriasis</b>	Acitretin	18%	6%	3%
	Cyclosporin	18%	9%	–
	<b>Methotrexate</b>	<b>59%</b>	<b>76%</b>	<b>82%</b>
	Psoralen UVA phototherapy	0%	–	–
	Acitretin + psoralen UVA phototherapy	0%	–	–
	Narrowband UVB phototherapy	3%	3%	–
	Apremilast (PDE-4 inhibitor)	6%	3%	–

Consensus regarding prescription is shown in bold.

– Where consensus was reached regarding the prescription or non-prescription of a given treatment, the question was not asked again in the subsequent round.

from systematic research' [22]. Thus, different sources and methods are necessary to increase the level of certainty at the individual level: meta-analyses, RCTs, observational real-world data, and Delphi consensus statements. Second, few RCTs are available for non-biological systemic treatments (e.g. cyclosporin, acitretin, methotrexate, UVB and psoralen/UVA phototherapy), and no systematic review can overcome the lack of data. Third, patients included in RCTs are a selected population and it is thus difficult

to generalize the results [23] or extend them to specific populations. Several comorbidities and clinical profiles were pinpointed in our Delphi study by the experts, leading to specific choices, e.g. active or recent cancer or pregnancy. Fourth, the Delphi method addressed clinical forms that are not usually explored in clinical trials but are encountered in clinical practice. For example, we highlighted the notion that erythrodermic, hyperkeratotic, pustular, and palmoplantar psoriasis may benefit from treatment



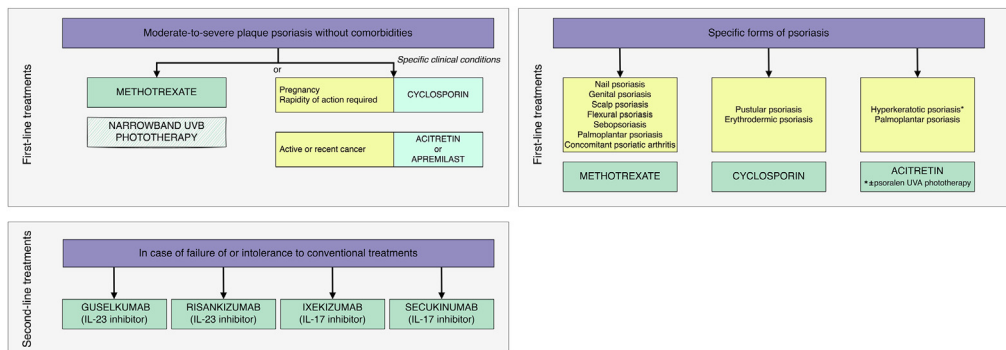


Fig. 1. Decision-making algorithm based on expert consensus for treatment selection for moderate-to-severe cutaneous psoriasis in adults.

options other than those used for plaque psoriasis. Thus, even if the supporting evidence is lower for patients with specific clinical forms or medical profiles, the Delphi method is one of the best ways to bridge the gap between evidence-based and experience-based medicine. In a period during which the number of effective treatments for psoriasis is constantly increasing, preparing consensus statements about the particular value of each drug can guide clinicians and contribute to the provision of more personalized medicine.

This Delphi consensus study presents several strengths. First, a key feature of the method is anonymity among participants to avoid bias through dominant individuals or group pressure to conform to or adopt any given viewpoint. Second, participants were recruited from among eminently qualified individuals and decision-makers in the field of psoriasis in France. The panel had experience in both hospital and private practice, thus providing both clinical and academic expertise. Third, we attained a high completion rate, despite the large number of proposals for which answers were mandatory. Lastly, we strictly followed the quality indicators of the Delphi method for the definition of a consensus and completion of the Delphi process [11,24].

There were nevertheless some limitations. First, no systematic review was performed, and no synthesis of the available literature was provided for the participants. However, a systematic review up to October 2021 was performed using the Cochrane database for the network meta-analysis [6]. The participants were recruited as experts and were thus assumed to be acquainted with the available knowledge in the field of psoriasis. In addition, the attention paid to specific studies may have biased their account of what they actually do in clinical practice. Second, we limited the recruitment of experts to France, where biological agents are authorized and reimbursed as second-line therapies due to failure of or a contraindication to a systemic non-biological treatment or phototherapy [25]. The generalizability of the results thus depends on regulatory frameworks across different countries. Third, our chosen criteria for consensus were strict (over 80% agreement), whereas a lower threshold would have provided consensus on the prescription of a wider range of drugs. However, our aim was to prioritize a small number of drugs so as to inform clinicians about the best therapeutic practice. Lastly, we did not include the newly authorized IL-17 inhibitor bimekizumab, as it was not available in France at the date of the Delphi process. A new Delphi process should be conducted within the next 3 years to update the present data.

To conclude, the treatment of psoriasis is a fast-evolving field requiring frequent updates of published guidelines and RCTs exploring new therapeutic strategies targeting complete remission as well as maintenance. Furthermore, due to (i) the limited generalizability of the results of RCTs, (ii) the availability of few or no

RCTs for most systemic non-biological treatments, and (iii) the availability of few or no RCTs for certain forms of psoriasis, we believe that the Delphi method complements systematic reviews in providing real-time and real-world guidelines [26].

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### Conflicts of interest

Appendix 1, supplementary material available online.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.annder.2024.103287>.

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