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REVIEW ARTICLE

Evidence-based recommendations on topical treatment and phototherapy of psoriasis: systematic review and expert opinion of a panel of dermatologists

C. Paul,[†] A. Gallini,[‡] E. Archier,[§] E. Castela,[¶] S. Devaux,[†] S. Aractingi,[**] F. Aubin,[††] H. Bachelez,[‡‡] B. Cribier,[§§] P. Joly,[¶¶] D. Jullien,[***] M. Le Maître,[†††] L. Misery,[‡‡‡] M.-A. Richard,[§] J.-P. Ortonne[¶]

[†]Dermatology Department, Paul Sabatier University, Toulouse, France
[‡]UMR 1027 INSERM – Université Paul Sabatier, Toulouse, France
[§]Aix-Marseille Univ, UMR 911, INSERM CRO2 and Dermatology Department, Timone Hospital, Marseille, France
[¶]Dermatology Department, Nice University, L'Archet II Hospital, Nice, France
[**]Dermatology Department, Tenon Hospital, APHP and Paris 6 University, Paris, France
[††]Dermatology Department, Franche Comté University, EA3181, IFR133, University Hospital, Besançon, France
[‡‡]Dermatology Department, Saint-Louis Hospital, Paris, France
[§§]Dermatology Department, University Hospital, Strasbourg, France
[¶¶]Dermatology Department, University Hospital, INSERM U 905 University of Rouen, France
[***]Dermatology Department, Edouard Herriot Hospital, Lyon, France
[†††]Dermatologist, Caen, France
[‡‡‡]Dermatology Department, University Hospital, Brest, France
*Correspondence: Carle Paul. E-mail: paul.c@chu-toulouse.fr

Abstract

Background Although topical treatments and phototherapy are available for more than 40 years, there is a paucity of evidence-based recommendations regarding their use.

Objectives The aim of this work was to develop evidence-based recommendations on topical treatments and phototherapy in psoriasis for daily clinical use.

Methods A scientific committee selected clinically relevant questions on efficacy and safety of topical agents and phototherapy in psoriasis. This selection was made using the Delphi method. A systematic literature search was performed in Medline, Embase and the Cochrane Library. The articles selected for analysis were reviewed and the level of evidence was appraised according to the Oxford Levels of Evidence. An Expert consensus meeting took place in June 2011, including 42 dermatologists. Recommendations for use of topical treatments and phototherapy were made during interactive workshops where the evidence was presented and discussed. Agreement among participants was assessed on a 10-point scale. The participants systematically assessed the impact of the recommendations on clinical practice.

Results A total of 3555 references were identified, among which 312 articles were included in the systematic reviews. Three recommendations were issued on phototherapy including both PUVA and narrow-band UVB. The recommendations related to administration schedule, clearance rate and risk of side-effects. The mean agreement between participants was good varying from 8.5 to 9.5. Six recommendations were issued on topical treatments focusing on administration schedule, clearance rate, risk of side-effects, cost-effectiveness and measures to improve treatment adherence. The mean agreement between participants varied from 7.3 to 9.9.

Conclusions These recommendations for the use of topical agents and phototherapy in psoriasis are evidence-based and supported by a panel of dermatologists. The next step will be to disseminate these recommendations and assess the opinion of physicians who were not involved in generating the recommendations.

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Conflicts of interest

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Introduction

Treatment of psoriasis has changed dramatically in the past 10 years with the recognition of high disease burden and the availability of multiple treatment options.[1,2]

Topical agents and phototherapy frequently represent first-line agents in the clinic for the management of mild and moderate psoriasis. Topical treatments include vitamin D analogues, topical corticosteroids, tar-based preparations, dithranol, salicylic acid and topical retinoids. Although systematic reviews do exist concerning topical treatments of psoriasis, there is a lack of evidence-based recommendations on optimal use, treatment strategy and selection of first-line agent based on efficacy and safety.[3]

Phototherapy of psoriasis has been used for more than 50 years. Several treatment recommendations on the use of phototherapy in psoriasis have been issued.[4–7] Few of them were elaborated following systematic appraisal of available literature and the level of heterogeneity is high. There are wide variations in dosimetry and treatment strategy between phototherapy specialists.[8]

The objectives of the present work were to elaborate practical recommendations for the use of topical treatments and phototherapy in psoriasis, based on systematic literature review and expert opinion of a panel of dermatologists with vested interest in psoriasis care.

As a first step, clinically relevant questions selected by the steering committee were subjected to systematic reviews. These questions addressed the use of topical treatments and phototherapy in psoriasis including efficacy, treatment modalities and safety. The frequency of non-adherence to topical agents and the strategies to improve adherence were also investigated. The results of the systematic reviews are presented along with the present article.[9–15] As a second step, a group of dermatologists with special interest in psoriasis care were consulted to formulate recommendations relevant to clinical practice according to a methodology described previously.[16,17]

Methods

In November 2010, the 11 psoriasis experts from the scientific committee (CP, SA, FA, HB, BC, PJ, DJ, MLM, LM, MAR, JPO) selected nine clinically relevant questions regarding topical treatments and phototherapy of psoriasis (Table 1). These questions were generated using a Delphi voting process.

A bibliographic team including a statistician (AG), three dermatologists (EA, EC, SD) and their mentors (MAR, JPO, CP) was nominated to conduct systematic reviews addressing the questions selected during the Delphi procedure.

Each systematic literature review was conducted in accordance with the updated guidelines of the Cochrane Collaboration.[18] Each clinical question was rephrased according to the PICO-method: The *Population* was defined as adult with psoriasis, and *Interventions, Comparisons* and *Outcomes* were specifically defined for each question.[19]

Comprehensive search strategies were developed in collaboration with experienced librarians, including search terms for Narrow Band-UVB therapy (NB-UVB), Psoralen + UltraViolet light-A therapy (PUVA), corticosteroid, calcipotriol, psoriasis, randomized controlled trial in adults and specific key words. Publication languages were restricted to French and English. The search included articles published since 1980. Medline, Embase and the Cochrane Library were searched. Additional references were identified via hand searches. The number of articles found and the articles selected for each topic are detailed in Table 2. Articles were selected applying pre-defined inclusion and exclusion criteria and their methodological quality was graded according to the Levels of Evidence defined by the Oxford Centre for Evidence-Based Medicine [http://www.cebm.net/index.aspx?o = 1025].

In each selected article, relevant data were extracted and when appropriate, meta-analyses were performed using random effects models.

The results of the systematic reviews were summarized for presentation and reviewed by the scientific committee. In a consensus meeting, 42 dermatologists with interest in psoriasis diagnosis and treatment reviewed the evidence available for each question in group workshops. They proposed a set of clinical recommendations addressing the initial clinical questions. At the end of these workshops, the scientific committee combined the proposals to produce nine recommendations. This final set of recommendations

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Table 1 Selected questions for each topic

Domains	Questions
Phototherapy	What is the respective efficacy of NB-UVB and PUVA (Psoralen + UVA Light)] in the treatment of adult psoriasis? What are the risks of skin cancer with PUVA and NB-UVB and is it possible to define a maximum number of phototherapy sessions not to be exceeded in a lifetime, according to the phototype? Are there other risks identified with phototherapy: risk of ocular damage, lentigines and photoageing?
Topical corticosteroid	What are the optimal treatment modalities with topical corticosteroids in psoriasis? What is the safety profile of long-term treatment with topical steroids in psoriasis? Risk of hypothalamic–pituitary–adrenal suppression, atrophogenicity
Topical vitamin D analogues and combination Vit D and steroid	What are the optimal treatment modalities with topical vitamin D analogues and with the combination of a topical vitamin D analogue and a topical steroid in psoriasis?
Other topical agents	What are the optimal treatment modalities with tazarotene, salicylic acid, dithranol and tars? in psoriasis
Compliance	What is the level of compliance with topical treatments in psoriasis?
First line topical therapy	Based on efficacy data, adherence and cost, is there a topical treatment of plaque psoriasis that can be recommended as first-line agent (excluding face and skin folds)?

Table 2 Results of the systematic literature search for each topic

Recommendation (number and topic)	References retrieved by systematic literature search (*n*)	Articles included in the systematic reviews (*n*)
1. Phototherapy – efficacy	773	29
2. Phototherapy – risk of skin cancer	243	49
3. Phototherapy – other risks Including:	441	
a. Ocular risk	30	13
b. Photoageing	14	6
c. Lentigines	23	13
4. Topical steroids – treatment modalities	1269	71
5. Topical steroids – safety	1269	27
6. Vit D – Vit D and topical steroids	253	51
7. Other topical agents	514	9
8. Compliance	62	22

was then presented to the group in a plenary session for final discussion and voting. The level of agreement was measured for each recommendation on a 10-point visual analogue scale (1 = no agreement, 10 = full agreement).[20] The potential impact of the recommendations on participants' clinical practice was evaluated by asking the participants to choose one of the following statements for each recommendation: 'this recommendation will change my practice'; 'this recommendation will not change my practice as it is already in full accordance with my practice'; 'this recommendation will not change my practice as I don't want to apply this recommendation in my practice'. Subsequently, the grade of each recommendation was assessed according to the Oxford Levels of Evidence.

Results

The nine recommendations are listed in Table 3, with the corresponding Level of Evidence and grade of recommendation. The mean level of agreement among experts for the recommendations was 8.64 (range from 7.26 to 9.98). The impact of the recommendations on the physicians' practice is detailed in Table 4.

Phototheraphy

The systematic literature review on this topic is presented in two accompanying papers and a letter (9, 10, 11).

A total of 773 references were identified of which 29 randomized controlled studies were selected and analysed. Three studies compared directly PUVA and NB-UVB.[21–23] No randomized controlled study directly compared different dosing strategies and frequency of application. Initial UV dose can be determined according to phototype, or according to the minimal erythemal dose (MED). Alternatively, it can be a fixed dose for all patients. Different protocols do exist regarding dose escalation with no obvious differences in efficacy between protocols. Clearance with phototherapy was estimated to range between 60 and 100% for PUVA, and between 40 and 100% with NB-UVB. The meta-analysis confirmed

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Table 3 Recommendations

Recommendations	Agreement Mean (0–10)
What is the respective efficacy of NB-UVB and PUVA (Psoralen + UVA Light)] in the treatment of adult psoriasis? PUVA is more effective than NB-UVB. It has a response rate of approximately 80% compared with 70% for NB-UVB (grade A). However, NB-UVB is preferred because of higher convenience except in case of very thick plaques (grade D) The optimal treatment regimen for phototherapy is 2–3 sessions per week (grade A). Between 20 and 30 treatment sessions are generally required for clearance (grade A). An absence of improvement after 30 sessions is considered as a treatment failure (grade D) The starting UV dose and the increases in dosage are defined according to phototype and tolerability (grade A) Topical treatments should not be applied less than 30 min before a phototherapy session (grade D)	8.80
What are the risks of skin cancer with PUVA and NB-UVB and is it possible to define a maximum number of phototherapy sessions not to be exceeded in a lifetime, according to the phototype? The risk of skin cancer is significantly increased with PUVA and there is a theoretical risk with NB-UVB (grade B). The number of cumulative (PUVA/NB-UVB) sessions during a lifetime must not exceed 250–300 (grade D)	8.50
Are there other risks identified with phototherapy? There is no increased risk of cataract associated with phototherapy provided that ocular protection measures are followed (grade C) Given the risk of photoageing, facial protection is recommended during sessions (grade D) Phototherapy should be discontinued when PUVA lentigines develop (grade D)	9.53
What are the optimal treatment modalities with topical steroids in psoriasis? As monotherapy topical steroids are recommended in psoriasis affecting a body surface area of ≤10%. The use of topical steroids on larger surface areas should be limited to exceptional circumstances Recommended initial treatment comprises the application of a potent or superpotent topical steroid once a day, for 4 weeks, with a maximum weekly dose of 30 g The aim is to achieve an improvement of 75% in severity at the end of the 4-week induction phase Occlusion is recommended for thick plaques and for palmar and plantar psoriasis Low and medium potency topical steroids are indicated only for psoriasis of the face and skin folds Medicinal preparations have no role in the treatment of psoriasis (grade D) Topical steroids may be applied twice weekly as maintenance treatment on the lesions sites (grade D) A dermatological review should be carried out after 6–12 weeks (grade D)	7.93
What is the safety profile of long-term treatment with topical steroids in psoriasis? The risk of skin infection during treatment with topical steroids is very low (grade D) When used according to recommendations, there is no risk of skin atrophy. The risk of significant systemic absorption and HPA axis suppression is very low (grade A)	9.98
What are the optimal treatment modalities with topical vitamin D analogues and with the combination of a topical vitamin D analogue and a topical steroid in psoriasis? As monotherapy, the combination of a vitamin D analogue and a topical steroid is recommended in psoriasis affecting a body surface area of ≤10%. It must be used sparingly over more extensive areas. Induction treatment: The efficacy of the combination between a vitamin D analogue and a topical steroid is higher than a vitamin D analogue alone, with a 50% success rate (grade A)- It should be applied once a day for 4 weeks (grade A) The recommended maximal dose for an affected body surface area of 10% is ≤2 × 60 g tubes per month (grade D) Vitamin D analogues as monotherapy are not indicated as induction treatment except for the face and skin folds (grade D) Maintenance therapy: The combination of a vitamin D analogue and a topical steroid may be applied twice weekly as maintenance treatment on the lesions site (grade A) The correct use of vitamin D analogues does not expose the patient to hypercalcemia following application to a skin surface area of ≤30% (grade A)	8.76
What are the optimal treatment modalities with tazarotene, salicylic acid, dithranol and tars in psoriasis? Tazarotene can be used sparingly and over a limited surface area in association with topical steroids for resistant plaques (grade A) Salicylic acid can be proposed at a concentration ≥5% as adjunct treatment for thick, limited psoriatic lesions (grade D) Dithranol and tars are no longer used in modern practice (grade D)	8.36
What is the level of compliance with topical treatments in psoriasis? Short-term treatment compliance is inadequate with approximately 50% of the recommended applications effectively performed (grade C) The following measures are recommended to improve compliance (grade D): Limit the number of products and the complexity of the prescription Limit the use of topical agents to a surface area of 10% or less Take into account the type and location of the lesions Inform the patient and involve him/her in the choice of treatment (molecule, formulation) Take into account the patient's objectives and lifestyle, and boost motivation Introduce a regular follow-up program Explain to the patient the different phases of topical treatments: induction phase and maintenance phase	8.62

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Table 3 (Continued)

Recommendations	Agreement Mean (0–10)
Based on efficacy data, adherence and cost, is there a topical treatment of plaque psoriasis that can be recommended as first-line agent (excluding face and skin folds)? The recommended first-line induction treatment for plaque psoriasis is a combination of a vitamin D analogue and a topical steroid (grade D) The recommended first-line induction treatment for scalp psoriasis can be either a combination of a vitamin D analogue and a topical steroid or a topical steroid alone (grade A)	7.26

Table 4 Impact of the recommendations on the physicians' practice

Recommendations (number and topic)	The recommendation will change my practice (%)	The recommendation is in full accordance with my practice (%)	I do not want to apply this recommendation in my practice (%)
1. Phototherapy efficacy	10.9	84.8	4.3
2. Phototherapy – risks of skin cancer	13.0	80.4	6.5
3. Phototherapy – other risks	26.1	71.7	2.2
4. Topical steroid –modalities for use	27.3	56.8	15.9
5. Topical steroid – safety	0.0	97.8	2.2
6. Vit D – Vit D and steroid	17.5	80.0	2.5
7. Other topical agents	9.1	70.5	20.5
8. Compliance	17.9	74.4	7.7
9. First line topical therapy	4.7	65.1	30.2

the superior efficacy of PUVA vs. NB-UVB in clearing psoriasis [(OR 2.79) 95% CI (1.40-5.55)].

Recommendation What is the respective efficacy of NB-UVB and PUVA (Psoralen + UVA Light)] in the treatment of adult psoriasis?

1 PUVA is more effective than NB-UVB. It has a response rate of approximately 80% compared with 70% for NB-UVB (grade A). However, NB-UVB is preferred because of higher convenience except for very thick plaques (grade D).
2 The optimal treatment regimen for phototherapy is 2–3 sessions per week (grade A).
3 Between 20 and 30 treatment sessions are generally required for clearance (grade A). An absence of improvement after 30 sessions is considered a treatment failure (grade D).
4 The starting UV dose and increases in dosage are defined according to phototype and tolerability (grade A).
5 Topical treatments should not be applied less than 30 min before a phototherapy session (grade D).

Experts agreement (mean): 8.80/10

Forty-nine articles were selected to answer the question about risk of skin cancer and the maximum number of sessions not to be exceeded in a lifetime. Most of them (45) concerned PUVA, with 10 prospective studies analysed. The risk of squamous cell carcinoma (SCC) and the risk of basal cell carcinoma (BCC) increase with the number of PUVA sessions. The risk appears to be superior in the cohort from the United States [24] as compared with the European cohorts.[25–27] This could be explained by differences in protocols or in patient phototypes. In Europe short-term treatment with higher doses was preferred over long-term treatment. A slightly increased risk of melanoma was described in the US cohort [28] but not in the three European studies.[25–27] There are few studies investigating the risk of skin cancer with NB-UVB. None of them established a link between increased risk of skin cancer and treatment with NB-UVB.

Recommendation

What are the risks of skin cancer with PUVA and NB-UVB and is it possible to define a maximum number of phototherapy sessions not to be exceeded in a lifetime, according to the phototype?

The risk of skin cancer is significantly increased with PUVA and there is a theoretical risk with NB-UVB (grade B). The number of cumulative (PUVA/NBUVB) sessions during a lifetime must not exceed 250–300 (grade D).

Experts agreement (mean): 8.50/10

The other risks identified with phototherapy were risk of ocular damage, risk of lentigines and accelerated photoageing.

Thirteen articles on PUVA evaluated the risk of ocular damage; there was no study with NB-UVB. The frequency of lens abnormalities varied from 0 to 13.5%, the highest rate was found in the American PUVA follow-up study.[29] In this cohort, PUVA was also associated with a higher risk of cataract, although the increased risk was not confirmed by Malanos *et al.*[30]

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Thirteen studies, two prospective and 11 retrospective studies with a follow-up varying between 1 and 17 years, evaluated the frequency of PUVA lentigines. Between 40 and 50% of patients receiving PUVA therapy experienced PUVA lentigines, the risk being associated with the number of PUVA sessions.

Analysis of the six studies investigating the risk of photoageing with PUVA therapy did not allow for exact risk quantification. There was no study investigating the risk of photoageing with NB-UVB. Therefore, the recommendation on risk of photoageing was exclusively formulated based on the experts experience.

Recommendation

1 Are there other risks identified with phototherapy?
2 There is no increased risk of cataract associated with phototherapy provided that ocular protection measures are followed (grade C).
3 Given the risk of photoageing, facial protection is recommended during sessions (grade D).
4 Phototherapy should be discontinued when PUVA lentigines develop (grade D).

Experts agreement (mean): 9.53/10

Topical steroids

The systematic literature review on this topic is presented in two accompanying papers (12,13).

Limited evidence was found in the literature to establish treatment recommendations on the use of topical steroids in psoriasis. Of 1269 references identified, only 71 satisfied the selection criteria. There was a large heterogeneity in studies and a wide dispersion in efficacy results. Most of the studies were old and did not comply with the CONSORT criteria about reporting results of randomized controlled studies.[31] No clear differences between molecules could be identified and even for the same molecule the reproducibility of results was questionable. There was limited data on dosing and maintenance treatment strategies. Only one study [32] compared fluocinonide once vs. four times daily and failed to show a difference in efficacy, one study [33] evaluated occlusion dressing on psoriasis clearance and concluded on the advantages of occlusion for thick plaques. Only one randomized controlled trial [34] compared maintenance treatment with betamethasone dipropionate three times weekly to placebo and concluded on the superiority of the topical steroid maintenance regimen at 6 months.

In terms of safety, the analysis focused on 13 studies evaluating the impact of topical corticosteroid treatment on hypothalamo-pituitary axis (HPA) and 13 studies measuring skin atrophy. The risk of skin infection could not be evaluated. The literature quality was limited: the number of patients studied was small and the follow-up was short. Fourteen studies, published in 13 selected articles were analysed to evaluate the effects of topical steroids on HPA. The effect on cortisol varied between studies. A reduction of baseline cortisol level of up to 48% was shown. To evaluate steroid induced skin atrophy 13 articles were analysed. Few studies specifically evaluated skin atrophy with prospective state of the art methodology including clinical scores and echography and only two studies [35,36] reported on a follow-up of 6 months to 1 year. The incidence of reported skin atrophy was below 5%. The literature is reassuring but does not reflect the reality due to the short follow-up.

The following recommendations on topical steroids treatment were issued, mostly based on expert opinion:

Recommendation What are the optimal treatment modalities with topical corticosteroids in psoriasis?

As monotherapy topical steroids are recommended in psoriasis affecting a body surface area of ≤10%. The use of topical steroids on larger surface areas should be limited to exceptional circumstances.

1 Recommended initial treatment comprises the application of a potent or superpotent topical steroid once a day, for 4 weeks, with a maximum weekly dose of 30 g. The aim is to achieve an improvement of 75% in severity at the end of the 4-week induction phase. Occlusion is recommended for thick plaques and for palmar and plantar psoriasis. Low and medium potency topical steroids are indicated only for psoriasis of the face and skin folds. Medicinal preparations have no role in the treatment of psoriasis (grade D).
2 Topical steroids are applied twice weekly as maintenance treatment on the lesions sites (grade D).
3 A dermatological review should be carried out after 6–12 weeks (grade D).

Experts agreement (mean): 7.93/10

Recommendation What is the safety profile of long-term treatment with topical steroids in psoriasis?

1 The risk of skin infection during treatment with topical steroids is very low (grade D).
2 When used according to recommendations, there is no risk of skin atrophy. The risk of significant systemic absorption and HPA axis suppression is very low (grade A).

Experts agreement (mean): 9.98/10

Topical vitamin D analogue and combination of a topical vitamin D analogue and a topical steroid

The systematic literature review on this topic is presented in an accompanying paper.[14]

Of 253 articles, 51 were selected: 19 articles on topical vitamin D analogue associated with topical steroids, 11 on topical vitamin D analogue alone, seven on tolerability, nine on topical vitamin D analogue treatment for scalp psoriasis, two on topical vitamin D analogue treatment for intertriginous psoriasis, three on quality of

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life. For the combination of a topical vitamin D analogue and a topical steroid, the treatment success rate defined by 'clear or almost clear' or PASI 90 varied from 27.2 to 55.3% at 4–8 weeks. The treatment success rate for topical vitamin D analogue monotherapy varied between 4% and 40.7%. The meta analysis showed that the probability of success is twice higher with the combination with a topical steroid as compared with the vitamin D analogue monotherapy (OR= 2.09 95% CI 1.47–2.96). Concerning safety, the research focused on hypercalcemia and skin atrophy. Safety was the main topic of seven articles.[36–42] No case of hypercalcemia was reported. Three other studies[43–45] reported transient hypercalcemia without any clinical implication, except in two patients for whom the topical vitamin D analogue was stopped. Skin atrophy was reported in two studies[36,46]

Only few studies investigated long-term treatment therefore no conclusion could be drawn. It was not possible to answer to the question on maximum dose of topical vitamin D analogue not to be exceeded with the systematic literature review. So, the dosage recommendation was based on the body area to be treated.

Recommendation What are the optimal treatment modalities with topical vitamin D analogues and with the combination of a topical vitamin D analogue and a topical steroid in psoriasis?

As monotherapy, the combination of a vitamin D analogue and a topical steroid is recommended in psoriasis affecting a body surface area of ≤10%. It must be used sparingly over more extensive areas.

1 Induction treatment: The efficacy of the combination between a vitamin D analogue and a topical steroid is higher than a vitamin D analogue alone, with a 50% success rate (grade A). It should be applied once a day for 4 weeks (grade A). The recommended maximal dose for an affected body surface area of 10% is ≤2 × 60 g tubes per month (grade D). Vitamin D analogues as monotherapy are not indicated as induction treatment except for the face and skin folds (grade D).
2 Maintenance therapy: The combination of a vitamin D analogue and a topical steroid is applied twice weekly as maintenance treatment on the lesions site (grade A).
3 The correct use of vitamin D analogues does not expose the patient to hypercalcaemia following application to a skin surface area of ≤30% (grade A).

Experts agreement (mean): 8.76/10

Other topical agents

Mason RA *et al.* published in 2009 a Cochrane review on topical treatments of psoriasis.[3] Their objectives were to compare the effectiveness, tolerability and safety of topical treatments for chronic plaque psoriasis, relative to placebo and they also compared vitamin D analogues with other topical treatments. The research performed by EC, to answer the question addressed by the Scientific Committee, allowed to update this review with randomized clinical trials published after 2008 regarding tazarotene, salicylic acid and tar. Eight additional articles were found. Tazarotene efficacy was evaluated in 4 RCT. About 50% of patients treated with tazarotene experienced a 50% or higher improvement in severity score with no differences between formulations. Few studies measured the efficacy of salicylic acid. Salicylic acid was usually applied in combination with a topical steroid with a study showing a slight improvement in efficacy as compared with topical steroids monotherapy.[47] Use of tar has progressively been abandoned.

Recommendation What are the optimal treatment modalities with tazarotene, salicylic acid, dithranol and tars in psoriasis?

1 Tazarotene can be used sparingly and over a limited surface area in association with topical steroids for resistant plaques (grade A).
2 Salicylic acid can be proposed at a concentration ≥5% as adjunct treatment for thick, limited psoriatic lesions (grade D).
3 Dithranol and tars are no longer used in current practice (grade D).

Experts agreement (mean): 8.36/10

Compliance

The systematic literature review on this topic is presented in an accompanying paper (15).

Twenty-two articles were selected and analysed. Some limitations in literature quality could be noted. There was a huge heterogeneity in methodology used in these studies and the data could not be compiled. Treatment duration was often too short to reliably measure compliance. Studies examined periods ranging from 10 days to 8 weeks in prospective studies. The adherence rate was found to vary between 50 and 100%. Adherence to treatment did not vary between the topical preparations.[48] The reasons for non-adherence and factors associated with poor adherence were compiled to produce the recommendation. Two studies showed that topical treatments of psoriasis were more frequently associated with poor adherence as compared with systemic treatments.[49,50] One study found adherence to be higher with topical therapy.[51] The most frequent reasons for non-adherence reported by patients were low efficacy of topical preparations, factors related to inconvenience, and fear of side-effects. A better adherence was associated with age, female sex, level of education, age at onset of the disease and severity; young patients and males appeared to be less compliant but being married, employed, and not paying for prescriptions were characteristics associated with increased medication adherence.

Strategies to improve adherence were outlined in few articles: therapeutic education was needed to improve adherence throughout a trustful relationship between physicians and patients [52–54]

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Patients aspired for a message of reassurance from the doctor about the use of the prescribed product, an idea of the timeframe and extent of beneficial results expected with treatment, and written instructions on medication use.[55]

Recommendation What is the level of compliance with topical treatments in psoriasis?

1 Short-term treatment compliance is inadequate with approximately 50% of the recommended applications effectively performed (grade C).
2 The following measures are recommended to improve compliance (grade D):
   (i) Limit the number of products and the complexity of the prescription.
3 Limit the use of topical agents to a surface area of 10% or less
4 Take into account the type and location of the lesions
5 Inform the patient and involve him/her in the choice of treatment (molecule, galenic)
6 Take into account the patient's objectives and lifestyle, and gather motivation
7 Introduce a regular follow-up program
8 Explain to the patient the different phases of topical treatments: induction phase and maintenance phase

Experts agreement (mean): 8.62/10

First line topical treatment

To determine the best available first line topical treatment to be recommended for plaque psoriasis, the available therapeutics options were compared in terms of cost effectiveness. Costs were determined by the French pharmacy price of topical products. The dose of topical agent to be used was determined using the frequency of application recommended in the summary of product characteristics and by applying the fingertip unit to calculate the amount to be used according to body surface area involved.[56] Efficacy data were derived from the systematic reviews on treatment success defined as PASI 90, disease absent or very mild, clear or almost clear psoriasis. Compliance was considered as similar for all topical agents.

Recommendation Based on efficacy data, adherence and cost, is there a topical treatment of plaque psoriasis that can be recommended as first-line agent (excluding face and skin folds)?

1 The recommended first-line induction treatment for plaque psoriasis is a combination of a vitamin D analogue and a topical steroid (grade D).
2 The recommended first-line induction treatment for scalp psoriasis can be either a combination of a vitamin D analogue and a topical steroid or a topical steroid alone (grade A).

Experts agreement (mean): 7.26 /10

Discussion

The present recommendations provide guidance on the optimal use of phototherapy and topical therapy in psoriasis based on systematic review of available evidence and practice from 42 experienced dermatologists. Three recommendations concern phototherapy of psoriasis. They provide flexibility regarding the number of sessions per week and the selection of doses according to phototype. In terms of safety, the recommendations put into perspective the risk of skin cancer with PUVA showing discrepancy between European and US cohort studies. The risk of skin cancer appears to be less with NB-UVB as compared with PUVA. The potential risk of cataract remains theoretical and is also put into perspective. For topical therapy, the recommendations provide with a limit in body surface area to be treated with topical therapy alone. Epidemiological studies[1,57] have shown that still many patients with moderate to severe psoriasis are treated with topical agents alone. The review of available evidence indicates that topical agents are extremely safe providing they are used according to the recommendations.

The major limitation of the current work is represented by the variability in the literature quality on topical therapy. Treatment outcome measures were not standardized in most studies which are >15 years old. Few studies evaluated the efficacy of topical agents on rare forms of psoriasis such as facial or intertriginous psoriasis. The vast majority of topical therapy studies deal with short-term treatment. This is of questionable relevance to psoriasis manifesting as a chronic disease. There is a need to produce better evidence regarding long-term treatment strategies with topical agents. This is of particular importance considering the issue of treatment adherence with topical agents as highlighted in the article by Devaux *et al.* Many patients experience discouragement with topical therapy of psoriasis in clinical practice. Therapeutic education programs with specialised nurses may help to increase treatment adherence in psoriasis in the future.[58] There is also a need to improve physician ability to write high quality prescription enabling patients to follow treatment recommendations as shown recently.[59]

As is frequently the case with therapeutic modalities developed more than 15 years ago, a large proportion of the proposed statements are only supported by grade D evidence[16]. Considering the extent of usage of topical therapy and phototherapy in psoriasis in the past 30 years, we believe the experience of expert physicians participating to this work palliated for this limitation. Indeed, the level of agreements of experts concerning these recommendations was high, with seven of nine recommendations obtaining a score between 8 and 10/10 on individual experts rating showing good to excellent agreement between experts. Of particular interest is the ability of the recommendations to change the practice of the participating physicians. There has been a considerable debate concerning the ability of medical literature to change the behaviour of physicians and observational studies have shown that there was a high discrepancy between recommendations formulated in

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guidelines and the actual behaviour of physicians in clinical practice or during teaching activities. We hope that the current recommendations which are both evidence based and supported by the input from a large group of practicing experts will be relevant to the future practice of physicians who are treating psoriasis patients with topical agents and phototherapy.

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