European Dermatology Forum

Methods report:
European S3-Guideline on the Systemic Treatment of Psoriasis vulgaris
Update Apremilast and Secukinumab

EDF in cooperation with EADV and IPC

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Methods report: European S3-Guideline on the systemic treatment of psoriasis vulgaris – Update Apremilast and Secukinumab – EDF in cooperation with EADV and IPC

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Abbreviations

APR	Apremilast
AWMF	German Association of Scientific Medical Societies
COI	Conflicts of interest
dEBM	Division of Evidence Based Medicine
EADV	European Association for Dermatology and Venereology
EDF	European Dermatology Forum
IPC	International Psoriasis Council
SEC	Secukinumab

Introduction

This document is the methods report for the **European S3-Guideline on the systemic treatment of psoriasis vulgaris – Update Apremilast and Secukinumab – EDF in cooperation with EADV and IPC**. The Update has been published in the Journal of the European Academy of Dermatology and Venereology.

Please use the following reference when citing the guideline: [to add]

The fast update was developed in accordance with the methods used for the European S3-Guideline on the systemic treatment of psoriasis vulgaris – Update 2015 [1] guided by the Cochrane Handbook for Systematic Reviews of Interventions and the GRADE working group [2, 3]. We also took into account the criteria of the Appraisal of Guidelines Research and Evaluation (AGREE II) Instrument [4]. Parts of this report may be identical to the previous methods report [1].

The objective of this fast update was to review and develop recommendations concerning two new treatment options for patients with psoriasis vulgaris, namely, secukinumab [5] and apremilast [6]. This is a treatment guideline primarily for dermatologist and general practitioners.

The members of the guideline development group and their respective affiliations are listed in table 1. The Division of Evidence-Based Medicine, Department of Dermatology, Charité - Universitätsmedizin Berlin; Berlin, Germany coordinated the process. The research team members conducted the evidence review and/or moderated the conference. The expert group was nominated by EDF, EADV, IPC. Patient representatives from the UK and Italy participated – each had one vote. However, no international patient organization could be identified to nominate representatives.

Table 1:

Name	**Affiliation**
research/systematic review team / information specialist	
Corinna **Dressler (CD)** Alexander **Nast** Stefanie **Rosumeck (SR)** Ricardo Niklas **Werner (RNW)**	Division of Evidence-Based Medicine, Department of Dermatology, Charité - Universitätsmedizin Berlin; Berlin, Germany
Gayle **van der Kraaij (GvK)**	Department of Dermatology, Academic Medical Center, Amsterdam, The Netherlands
Marlies **Wakkee (MW)**	Erasmus MC, Rotterdam, The Netherlands
Paula **van Lumig (PvL)**	Radboud University Nijmegen, The Netherlands
Expert group	
Esteban **Dauden**	Hospital Universitario de la Princesa, Madrid, Spain
Elke **de Jong**	University Medical Center Nijmegen St Radboud, Nijmegen, The Netherlands
Eugen **Feist**	Medizinische Klinik mit Schwerpunkt Rheumatologie u. klinische Immonologie, Charité - Universitätsmedizin Berlin, Berlin, Germany

Paolo **Gisondi**	University of Verona, Section of Dermatology and Venereology, Department of Medicine, Verona, Italy
Ray **Jobling**	Cambridge, UK
Mara **Maccarone**	Roma, Italy
Ulrich **Mrowietz**	Deptartment of Dermatology, Psoriasis-Center University Medical Center Schleswig Holstein, Kiel Germany
Anthony D. **Ormerod** (steering group)	Department of Dermatology, Aberdeen Royal Infirmary, Aberdeen, UK
Kim Alexander **Papp** (steering group)	Waterloo, Canada
Carle **Paul**	Department of Dermatology, Paul Sabatier University, Toulouse, France
Kristian **Reich**	Dermatologikum Hamburg, Hamburg, Germany
Philippe **Saiag** (steering group)	Service de Dermatologie, Hôpital Ambroise Paré Université Paris V, Boulogne, France
Catherine **Smith** (steering group)	Clinical Lead for Dermatology, Guys and St Johns Institute of Dermatology, St Thomas' Hospital foundation Trust, London, UK
Phyllis I. **Spuls** (steering group)	Department of Dermatology, Academic Medical Center, Amsterdam, The Netherlands
Toomas **Talme**	Section of Dermatology and Venereology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Huddinge, Stockholm, Sweden
Hok Bing **Thio**	Deptartment of Dermatology, Erasmus University, Rotterdam, The Netherlands
Peter **van de Kerkhof**	Department of Dermatology, University Hospital Nijmegen, Nijmegen, The Netherlands

Funding and Management of conflict of interests

The guideline development process was funded by the EDF. The expert panel did not receive any financial support or reimbursement for participation. Each expert panel member was obliged to submit a declaration of interest before the kick-off meeting and an update prior to the consensus conference. Conflicts of interests were discussed within the expert panel. Each declaration of interest can be found in appendix 2.

Methods

An internal protocol was develop *a priori* in order to answer the research question on the efficacy and safety of secukinumab or apremilast in patients with psoriasis vulgaris. The detailed research criteria are listed table 2.

Table 2: PICO framework

Patients	- Psoriasis vulgaris/ plaque type psoriasis (at least 80% of the trial participants had to meet this criteria) - Adults (as defined in the study)
Intervention	- Apremilast (any dose and any treatment regime) - Secukinumab (any dose ≥ 150mg and more than one dose had to be administered)
Comparator	- Placebo or head-to-head with any other systemic treatment for psoriasis

Outcome	- Efficacy outcomes: number of patients achieving PASI 75/90, % reduction in mean PASI/ final PASI score (mean and SD), number of patients achieving PGA 0 or PASI 100 (clearance/clear), number of patients achieving PGA 0/1 (clear/almost clear) - Safety outcome for induction and long-term therapy: number of patients withdrawn due to adverse events (AEs), number of patients with at least one AE, number of patients with at least one serious adverse event (SAE) - Patient reported outcomes: mean reduction in DLQI (mean and SD), number of patient with a DLQI <= 5, ➔ Time points for all of the above-listed outcomes: induction therapy (8 to 16 weeks) and long –term therapy (24 to 28 weeks) - Other: Time till onset of action - time until 25% of patients achieve a PASI 75 response, Time till onset of action- time until a 25% reduction of the mean baseline PASI is achieved, time to relapse after discontinuation of treatment, relapse rate at a given time point (as reported in publication)
Study type	- Randomized controlled trials only

Literature review

Secukinumab and Apremilast have been granted a marketing authorization on January 15th 2015[5, 6]. As this is an addition to an existing guideline, the same methodology was used and no search for further other guidelines had been conducted. The Dutch guideline had been updated just before the initiation of the work on the EU guidelines and synergies were generated for the evidence base.

A systematic literature search was conducted in Medline, Medline In-Process, Embase (all via OvidSP) and CENTRAL (Wiley) searching for primary data publications. Autoalerts for all four databases were activated. The search strategy for Medline can be found in appendix 1. We limited our search to randomized controlled trials; the searches were run since inception of database.

Selection and data extraction

Our primary interest were randomized controlled trials evaluating secukinumab or apremilast for psoriasis vulgaris reporting at least one efficacy outcomes listed in table 2. All hits identified in the literature search were imported into EndNote X7. We removed all duplicates prior to the title/abstract screening phase manually. The project team independently assessed records for inclusion at the title/abstract and the full-text screening stage. Two reviewers extracted the data independently using a standardized MS Excel sheet. Outcomes,

as listed in table 2, were extracted alongside with study characteristics and baseline data. In case of disagreements, a third reviewer (RNW) checked the data and issues were resolved in discussion. If conflicting data was published, we opted for the more conservative estimate.

Any relevant data for which only graphical representations were available, the software Engauge Digitzer was used to extract information.

Data transformation

For dichotomous and continuous outcomes, data was used as reported in the publications (no imputation). For continuous outcomes where no standard deviation(SD) was reported, the SD was calculated using the standard error or the confidence interval. If data was not reported in these formats, it could not be included in the statistical analysis.

We imputed the placebo arm data for long-term treatment as described in the methods report for the European S3-Guidelines on systemic treatment of psoriasis vulgaris [7].

We calculate time till onset of action for 1) time until 25% of patients achieved PASI 75 and 2) time until a 25% reduction of the mean baseline PASI is achieved. Detailed methods have been described elsewhere [8].

Data analysis

For all placebo-comparisons the different dosages were pooled. If studies included more than two arms, the groups were split in half for meta-analysis purposed. This way, participants would not be counted twice.

Review Manager [9] was used to calculate effect estimates and 95% confidence intervals (pairwise comparisons). We also calculated summary effect measures using random effect models not assuming a common effect size.

Assessment of the quality of the evidence

The quality of the evidence was assessed following the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system evaluating the evidence for five criteria using the GRADEpro Guideline Development Tool [4].

1. Risk of Bias: The Cochrane Risk of Bias Assessment Tool was used to assed the risk of bias on study level[10]. Downgrading depended on the methodological quality of the individual studies. A downgrade by 1 or 2 points was possible if several risk of bias categories had been assessed to be unclear and/or high.

2. Imprecision [11]: We evaluated imprecision based on the confidence interval (CI). If the CI crossed the line of no effect and the threshold(s) for minimal important difference (MID) we downgraded due to uncertainty of whether there is any difference. We also downgraded if the CI crossed only the MID threshold due to statistically significant difference of uncertain clinical importance. The MID is defined as the line of no effect ± 0.25 for risk ratios and for continuous outcomes where no other data was available, we used ½ of the standard deviation of the control group on both sides of the line of no effect. A very wide confidence interval was also a reason to downgrade.

For time till onset of action outcomes we downgraded twice because for the data calculated in secondary analyses no measures of variance were available.

3. Indirectness [12]: We downgraded by 1 point if baseline characteristics did not match the study inclusion criteria. We also downgraded whenever the study population was different from the population for which a recommendation was going to be developed by the expert panel.

4. Inconsistency [13]: We downgraded whenever study results were heterogeneous and the estimates differed and/or if, for example, an estimate was not included in the confidence interval of another subgroup or where confidence intervals had no or minimal overlap. A large I^2 also warranted downgrading due to methodological differences (I^2 result listed in footnotes).. Where only 1 study could be included, we did not downgrade.

5. Publication bias: Due to the limited number of publications, *publication bias* could not be assessed and we opted for the default option of 'no bias detected' [14].

Reasons for downgrading are listed as footnotes in the GRADE evidence profiles. An overview of the criteria used to evaluate the quality of the evidence and the different possible levels of the quality of evidence are show in table 3.

Table 3: Summary of the GRADE approach

Study design	Initial quality of body of evidence	Criteria that may decrease the quality	Criteria that may increase the quality	Quality of body of evidence	
RCT	high	- Risk of bias - Inconsistency - Indirectness - Imprecision - Publication	- Large effect - Dose response - Residual confoundi	High (++++)	We are very confident that the true effect lies close to that of the estimate of effect.
				Moderate (+++)	We are moderately confident in the effect estimate: The true effect is likely to be close to the

	bias	ng		estimate of the effect, but there is a possibility that it is substantially different.
			Low (++)	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
			Very low (+)	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

The final GRADE tables report the quality of the evidence in each comparison for each outcome separately. The relative effect is presented as a risk ratio including confidence interval and the anticipated absolute effect is presented as the risk difference, which refers to how many more or fewer patients achieve the outcome of interest compared to the control group.

Results

The literature search in four databases conducted on 03.02.2016 found 559 hits of which 173 duplicates were removed. Autoalerts were screened until 27.07.2016. An additional 14 hits were identified. Five reviewers (CD, SR, GK, MW, PvL) screened 400 title/abstract for inclusion. A total of 69 full text were evaluated using the same criteria (CD, SR, RNW). Fifty-two full text were excluded because: no additional data reported (41), no RCT (2), pooled data only (1) and other outcome (1). Hence, 16 full texts were included (see figure 1: Study selection flow chart). Each record was screened and extracted by two reviewers independently.

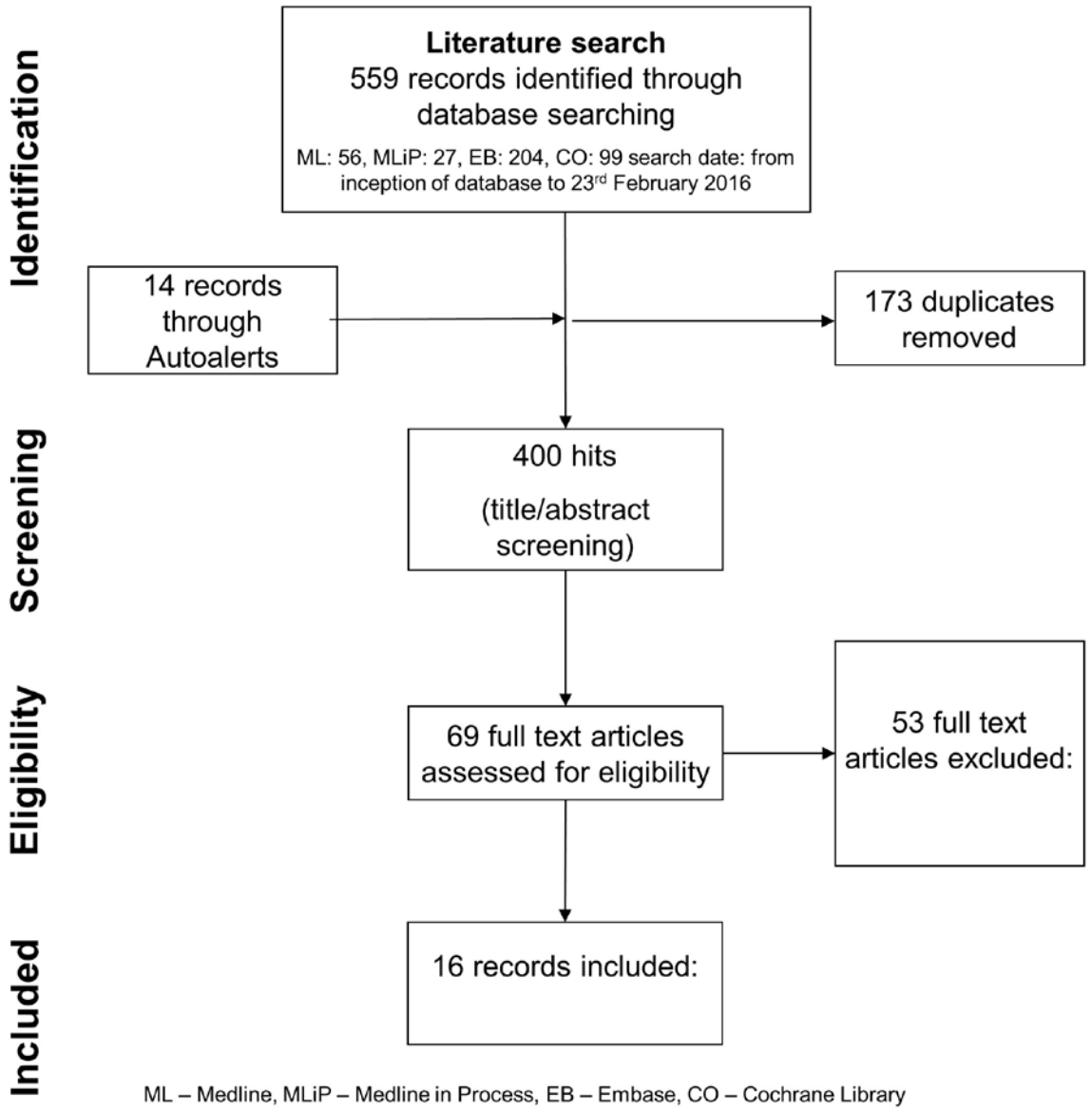

Figure 1: Study selection flow-chart

Data from 16 records were extracted and the quality of the evidence was evaluated for each comparisons. We summarized the evidence for each comparison in a short paragraph for inclusion in the guideline. For transparency, all GRADE evidence profiles are available as a supplement to the guideline.

Development of the recommendations

Prior to the consensus conference, the summary of the results of the evidence assessment was send to the expert group alongside a draft version of the guideline. The experts had first

prepared text passages, which could then be commented on or discussed during the consensus conference.

The consensus conference took place on November 2nd 2016. The telephone conference with screen sharing was moderated by Alexander Nast, MD, certified by the German Association of Scientific Medical Societies (AWMF) as Guidelines Advisor. Each expert group member was entitled to one vote. The review team (methodologists) did not vote. The nominal group technique was used to identify, discuss and agree upon recommendations.

The evidence was considered for the development of evidence-and consensus-based recommendations. Additionally, consensus-based recommendations for special patient populations were also developed.

In line with the 2015 EU psoriasis guideline, all consented passages are highlighted in grey throughout the document. Standardized languages was used when describing the direction and strength of the recommendations based on GRADE[15]:

1) strong recommendation for the intervention (“We recommend…” - ↑↑),

2) weak recommendation for the intervention (“We suggest…” ↑),

3) no recommendation (“We cannot make a recommendation with respect to….” ○),

4) weak recommendation against (“We suggest against…” ↓) and

5) strong recommendation against (“We recommend against…” ↓↓).

The results of the voting was document for each recommendation. The level of consensus can be distinguished by three cut-off points: >= 95% strong consensus, 75% - 94% fair consensus, and 50% to 74 % weak consensus.

The sections *Instruction for use and lab control* were voted on in four parts (pre, during, after and lab).

Review

Once the internal review process was completed, the guideline document, the methods report and the GRADE tables were available publically on the www.debm.de website from March 1st until March 29th 2017. Stakeholders were invited via email to comment. We received comments from ten stakeholders. All comments were sent to the author group for discussion. Each comment was replied to, and either the text in the guideline was changed or the comment was rejected (with reason). Replies were sent back to stakeholders.

Implementation, evaluation and updating

This European guideline should be adapted to the national level and hence, an evaluation of the implementation should be conducted on the national level too.

The guideline is an update to the European S3-guideline on the treatment of psoriasis necessary because these new interventions became available. The update expires January 2020.

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[1] Nast A, Gisondi P, Ormerod AD, Saiag P, Smith C, Spuls PI, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris - Update 2015 - Short version - EDF in cooperation with EADV and IPC. J Eur Acad Dermatol Venereol. 2015.

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[13] Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 7. Rating the quality of evidence--inconsistency. Journal of clinical epidemiology. 2011;64; 1294-1302.

[14] Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, et al. GRADE guidelines: 5. Rating the quality of evidence--publication bias. Journal of clinical epidemiology. 2011;64; 1277-1282.

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Appendix 1: Search Strategy Medline

1. exp Psoriasis/
2. psoriasis.mp.
3. 1 or 2
4. "secukinumab".ab,ti,nm.
5. "apremilast".ab,ti,nm.
6. 4 or 5
7. 3 and 6
8. Randomized Controlled Trials as Topic/
9. randomized controlled trial/
10. Random Allocation/
11. Double-Blind Method/
12. Single Blind Method/
13. clinical trial/
14. clinical trial, phase I.pt.
15. clinical trial, phase II.pt.
16. clinical trial, phase III.pt.
17. clinical trial, phase IV.pt.
18. controlled clinical trial.pt.
19. randomized controlled trial.pt.
20. multicenter study.pt.
21. clinical trial.pt.
22. exp Clinical Trials as topic/
23. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. (clinical adj trial$).tw.
25. ((singl$ or doubl$ or treb$ or tribl$) adj (blind$3 or mask$3)).tw.
26. Placebos/
27. placebo$.tw.
28. randomly allocated.tw.
29. (allocated adj2 random$).tw.
30. 24 or 25 or 26 or 27 or 28 or 29
31. 23 or 30
32. case report.tw.
33. letter/
34. historical article/
35. 32 or 33 or 34
36. 31 not 35
37. 7 and 36

Appendix 2: Declaration of Interest

		Dauden, Esteban	Dressler, Corinna	de Jong, Elke
1	**Work Under Consideration for these Guidelines**			
1.1	Grant	No	Institution: European Dermatology Forum	No
l1.2	Consulting fee or honorarium	No	No	No
1.3	Support for travel to meetings for the study or other purposes	No	No	No
1.4	Fees for participation in review activities such as data-monitoring boards, statistical analysis, end-point committees, and the like	No	Institution: European Dermatology Forum	No
1.5	Payment for writing or reviewing the manuscript	No	Institution: European Dermatology Forum	No
1.6	Provision of writing assistance, medicines, equipment, or administrative support	No	No	No
1.7	Other	No	No	No
2	**Relevant Financial Activities Outside Submitted Work**			
2.1	Board membership	Personally: Abott/Abbvie, Janssen-Cilag, Celgene, LEO, Lilly, Pharma, Novartis, Pfizer	No	No
2.2	Consultancy	No	No	Institution: (inter) national consultancies for companies manufacturin

				g treatments for prosiasis: Pfizer, AbbVie, Janssen
2.3	Employment	No	No	No
2.4	Expert testimony	No	No	No
2.5	Grants/grants pending	Institution: Abbott/Abbvie, Janssen-Cilag, Pfizer, MSD	No	Institution: companies manufacturing treatments for prosiasis for investigator initiated research: Pfizer, AbbVie, Janssen
2.6	Payment for lectures including service on speakers bureaus	Personally: Abbott/Abbvie, Janssen-Cilag, Lilly, Pfizer, MSD, LEO Pharma, Novartis, Celgene	No	Institution: companies manufacturing treatments for prosiasis: Pfizer, AbbVie, Janssen, MSD
2.7	Payment for manuscript preparation	No	No	No
2.8	Patents (planned, pending, or issued)	No	No	No
2.9	Royalties	No	No	No
2.10	Payment for development of educational presentations	No	No	Institution: AbbVie
2.11	Stock/stock options	No	No	No
2.12	Travel, accommodations, and meeting expenses unrelated to activities listed	No	No	No
2.13	Other (err on the side of full disclosure)	No	No.	No
3	**Other relationships**	No	No	No

		Feist, Eugen	Gisondi, Paolo	Jobling, Raymond	Van der Kraaij, Gayle	Van Lumig, Paula
1	**Work Under Consideration for these Guidelines**					
1.1	Grant	No	No	No	No	No
1.2	Consulting fee or honorarium	No	No	No	No	No
1.3	Support for travel to meetings for the study or other purposes	No	No	No	No	No
1.4	Fees for participation in review activities such as data-monitoring boards, statistical analysis, end-point committees, and the like	No	No	No	No	No
1.5	Payment for writing or reviewing the manuscript	No	No	No	No	No
1.6	Provision of writing assistance, medicines, equipment, or administrative support	No	No	No	No	No
1.7	Other	No	No	No	No	No
2	**Relevant Financial Activities Outside Submitted Work**					
2.1	Board membership	Personally: Novartis, Pfizer, BMS	No	No	No	No
2.2	Consultancy	No	No	No	No	No
2.3	Employment	No	No	No	No	No
2.4	Expert testimony	No	No	No	No	No
2.5	Grants/grants pending	No	No	No	No	No

2.6	Payment for lectures including service on speakers bureaus	Personally: Novartis, Pfizer, Abbvie, MSD, Celgene	Personally: Pfizer, Janssen, Abbvie, Merck Sharp, Dome	No	No	Received speaking and consulting fees from Wyeth and Schering-Plough in the past.
2.7	Payment for manuscript preparation	No	No	No	No	No
2.8	Patents (planned, pending, or issued)	No	No	No	No	No
2.9	Royalties	No	No	No	No	No
2.10	Payment for development of educational presentations	No	No	No	No	No
2.11	Stock/stock options	No	No	No	No	No
2.12	Travel, accommodations, and meeting expenses unrelated to activities listed	No	No	No	No	No
2.13	Other (err on the side of full disclosure)	No	No	No	Institution: Clinical studies (Janssen Cilag, Novartis, Celgene)	Carried out clinical trials for Abbott and Janssen-Cilag. Received reimbursement for attending conferences from Schering-Plough, Pfizer and Janssen.
3	**Other relationships**	No	No	No	No	No

	Maccarone, Mara	**Mrowietz, Ulrich**	**Nast, Alexander**	**Ormerod, Anthony**	**Papp, Kim**

1	**Work Under Consideration for these Guidelines**					
1.1	Grant	No	No	Institution: European Dermatology Forum	Novartis	No
1.2	Consulting fee or honorarium	No	No	No	Novartis	No
1.3	Support for travel to meetings for the study or other purposes	No	No	No	No	No
1.4	Fees for participation in review activities such as data-monitoring boards, statistical analysis, end-point committees, and the like	No	No	Institution: European Dermatology Forum	No	No
1.5	Payment for writing or reviewing the manuscript	No	No	Institution: European Dermatology Forum	No	No
1.6	Provision of writing assistance, medicines, equipment, or administrative support	No	No	No	No	No
1.7	Other	No	No	No	No	No
2	**Relevant Financial Activities Outside Submitted Work**					
2.1	Board membership	No	Personally: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Eli Lilly, Novartis, Dr. Reddy's, Xenoport	Personally (with relevance to Psoriasis): Boehringer Ingelheim (however none of BI's product was part of the guidelines),	No	AbbVie, Amgen, Astellas, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Merck (MSD), Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genz

						yme, UCB, Valeant
2.2	Consultancy	No	Personally: Almirall, Boehringer Ingelheim, Celgene, Eli Lilly, Formycon, Forward Pharma, Janssen, LEO Pharma, Novartis, Dr. Reddy's	No	Jansen, Eli-Lillley, Leo	AbbVie, Akros, Amgen, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, CanFite, Celgene, Dermira, Devonian, Dow Pharma, Eli Lilly, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo, Meiji Seika Pharma, Merck (MSD), Merck-Serono, Mitsubishi Pharma, Mylan, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant
2.3	Employment	No	No	No	No	No
2.4	Expert testimony	No	No	Personally: Sanofi Germany	No	No

2.5	Grants/grants pending	No	Institution: Abbvie, Almirall, Celgene, Forward Pharma, Novartis	Institution (with relevance to psoriasis) Pfizer, Lilly, Novartis	Jansen, Pfizer, Merk	AbbVie, Akros, Allergan, Amgen, Anacor, Astellas, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GSK, Janssen Kyowa Hakko Kirin, Leo, Medimmune, Merck (MSD), Merck-Serono, Mylan, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Stiefel, Takeda, UCB, Valeant
2.6	Payment for lectures including service on speakers bureaus	No	Personally: AbbVie, Almirall, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Eli Lilly, Medac, MSD, Novartis	Personally (with relevance to Psoriasis): Pfizer, Janssen	No	No
2.7	Payment for manuscript preparation	No	No	No	No	No

2.8	Patents (planned, pending, or issued)	No	No	No	Patents on Topical Nitric oxide	No
2.9	Royalties	No	No	No	No	No
2.10	Payment for development of educational presentations	No	No	No	No	AbbVie, Amgen, Astellas, Celgene, Devonian, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo, Merck (MSD), Novartis, Pfizer, Valeant
2.11	Stock/stock options	No	Personally: Forward Pharma	No	No	No
2.12	Travel, accommodations, and meeting expenses unrelated to activities listed	No	No	No	No	No
2.13	Other (err on the side of full disclosure)	No	No		No	No
3	**Other relationships**	No	No	No	Data monitoring committees Amgen	Scientific Officer: Akros, Anacor, Kyowa Hakko Kirin Steering Committee member: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck (MSD), Merck-Serono,

						Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, Valeant

		Paul, Carle	Reich, Kristian	Rosumeck, Stefanie	Saiag, Philippe	Smith, Catherine
1	**Work Under Consideration for these Guidelines**					
1.1	Grant	No	No	Institution: European Dermatology Forum	No	No
1.2	Consulting fee or honorarium	No	No	No	No	No
1.3	Support for travel to meetings for the study or other purposes	No	No	No	No	No
1.4	Fees for participation in review activities such as data-monitoring boards, statistical analysis, end-point committees, and the like	No	No	Institution: European Dermatology Forum	No	No
1.5	Payment for writing or reviewing the manuscript	No	No	Institution: European Dermatology Forum	No	No
1.6	Provision of writing assistance, medicines, equipment, or administrative support	No	No	No	No	No
1.7	Other	No	No	No	No	N/A
2	**Relevant Financial Activities Outside Submitted Work**					
2.1	Board membership	No: EADV (Secretary general)	Personally: AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac,	No	Personally/ institution: Roche, GSK, BMS, MSD, Pierre Fabre, Merk-Serono, Amgen, Novartis	No

			MSD, Novartis, Ocean Pharma, Pfizer, Takeda, Vertex			
2.2	Consultancy	Personally: Allmiral, Astellas, Pierre Fabre, Sanofi, Abbvie, Amgen, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer (Consultancy in the field of clinical research and data review)	Personally: AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Takeda, Vertex	No	Personally: Roche, GSK, BMS	No
2.3	Employment	No	No	No	No	No
2.4	Expert testimony	No	Personally: AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Takeda, Vertex	No	No	No

2.5	Grants/grants pending	Institution: GSK, Pfizer, Pierre Fabre (Grant for clinical research work)	Institution: Novartis, MEDA, Takeda	No	Institution: Roche	Departmental research funding from AbbVie, Pfizer, Novartis, GSK, Roche, Regeneron
2.6	Payment for lectures including service on speakers bureaus	Personally: Abbvie, Celgene, Pfizer (Lectures at scientific symposia) Janssen Lilly	Personally: AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Takeda, Vertex	No	Personally: Roche, GSK, BMS, MSD, Pierre Fabre, Merk-Serono, Amgen, Novartis	No
2.7	Payment for manuscript preparation	No	No	No	No	No
2.8	Patents (planned, pending, or issued)	No	No	No	No	No
2.9	Royalties	No	No	No	No	No
2.10	Payment for development of educational presentations	Personally: Abbvie (Psoriasis educational slides) Lilly	Personally: AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac, MSD,	No	Personally: Roche, NovartisK, MSD, Pierre Fabre, BMS	No

			Novartis, Ocean Pharma, Pfizer, Takeda, Vertex			
2.11	Stock/stock options	No	No	No	No	No
2.12	Travel, accommodations, and meeting expenses unrelated to activities listed	Personally: Janssen (Support for attending AAD 2012) Sanofi, Novartis	Personally: AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Takeda, Vertex	No	Personally: Roche, GSK, BMS, MSD, Pierre Fabre, Merk-Serono, Amgen, Novartis S	No
2.13	Other (err on the side of full disclosure)	No	No	No	No	No
3	**Other relationships**	No	No	No	No	No

		Spuls, Phyllis	Talme, Thomas	Thio, Hok Bing	van de Kerkhof, Peter	Wakkee, Marlies	Werner, Ricardo
1	**Work Under Consideration for these Guidelines**						
1.1	Grant	No	No	No	No	No	Institution: European Dermatology Forum
1.2	Consulting fee or honorarium	No	No	No	No	No	No
1.3	Support for travel to meetings for the study or other purposes	No	No	No	No	No	No
1.4	Fees for participation in review activities such as data-monitoring boards, statistical analysis, end-point committees, and the like	No	No	No	No	No	Institution: European Dermatology Forum
1.5	Payment for writing or reviewing the manuscript	No	No	No	No	No	Institution: European Dermatology Forum
1.6	Provision of writing assistance, medicines, equipment, or administrative support	No	No	No	No	No	No
1.7	Other	No	No	No	No	No	No
2	**Relevant Financial Activities Outside Submitted Work**						
2.1	Board membership	Institution: Leo-pharma (Dovobet), Novartis (Omalizu-ma), Anacor	Personal-ly: AbbVie, Novartie, Janssen, Pfizer	No	No	No	No
2.2	Consultancy	Consultancies in the past for Leopharma, Anacor, AbbVie and Novartis	No	Personally: Janssen, Novartis, TEVA, Biogen Idec, Abbvie, Celgene, Lilly	Institution: Celgene, Centocor, Allmirall, Amgen, Pfizer, Philips, Abbvie, Ely Lilly, Galderma,	No	No

					Novartis, Jansen Cilag, Leo Pharma, Sandoz		
2.3	Employment	No	No	No	No	No	No
2.4	Expert testimony	No	No	Personally: Janssen, TEVA	No	No	No
2.5	Grants/grants pending	Independent research grants In the past from Schering Plough and Leopharma	No	Institution: Pfizer, Celgene	Institution: Basilea GSK, Pfizer, Ely Lilly, Amgen, Abbvie, Philips Lighting, Jansen Cilag, Leo Pharma, Allmirall	No	No
2.6	Payment for lectures including service on speakers bureaus	No	Personally: AbbVie, MSD	Personally: MSD, Janssen, Novartis, Leopharma, Biogen Idec, Abbvie	Institution: Celgene, Allmirall, Amgen, Pfizer, Ely Lilly, Abbvie, Galderma, Novartis, Jansen Cilag, Leo Pharma	Janssen-Cilag	No
2.7	Payment for manuscript preparation	No	No	No	No	No	No
2.8	Patents (planned, pending, or issued)	No	No	No	No	No	No
2.9	Royalties	No	No	Personally: Elsevier	No	No	No
2.10	Payment for development of educational presentations	No	No	Personally: Astellas, Novartis	No	No	No
2.11	Stock/stock options	No	No	No	No	No	No
2.12	Travel, accommodations, and meeting expenses unrelated to activities listed	No	Personally: AbbVie, Janssen, Pfizer	Personally: Abbvie, Janssen, Lilly, Novartis,Galderma	Institution: Celgene, Pfizer, Abbvie, Ely Lilly, Galderma, Novartis,	Abbvie	No

					Jansen Cilag, Leo Pharma, Sandoz		
2.13	Other (err on the side of full disclosure)	Involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of psoriasis and atopic dermatiti	No	No	No	No	No
3	**Other relationships**	No	No	No	No	No	No