EUROGUIDERM GUIDELINE ON ATOPIC ECZEMA– METHODS REPORT

Version 1.0, June 2022

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Notes on use/Disclaimer

This is the methods report of the evidence and consenus based EuroGuiDerm Atopic Eczema Guideline.

Funding (standard) Statement

The development of this EuroGuiDerm guideline was funded through the EuroGuiDerm Centre for Guideline Development. The European Dermatology Forum is responsible for fundraising and holds all raised funds in one account. The EuroGuiDerm Team is not involved in fundraising or in the decision making on which guideline (GL) or consensus statement (CS) development is funded. The decisions on which GL/CS is funded are made by the EuroGuiDerm Board of Directors independently. The EDF or any other body supporting the EuroGuiDerm is never involved in the guideline development and had no say on the content or focus of the guideline.

Involving stakeholders and establishing the guideline subcommittee

In December and January 2019/2020, invitations were sent out to all EuroGuiDerm funding societies (n=12). Each society was asked to nominated a candidate to partake in the guideline development process, see Table 1. We also made public announcements to all European Dermatology Forum (EDF) members and used social media to call for participation.

The link to the EuroGuiderm standardized online declaration of interests form was sent via electronic mail to all chosen experts and each of them had to declare: 1) personal-financial interests (PF), 2) non-personal financial interests (NP-F), and 3) their personal non-financial interests (P-NF). The EuroGuiDerm Board of Directors made the final decision on which candidates may participate considering their self-reported PF interests. Experts were informed afterwards about the decision through e-mail.

TABLE 1: MEMBERS OF THE GUIDELINE DEVELOPMENT GROUP

Title	First name	Last name	Insitution	Expertise	Country	Role
	Arents	Bernd	European Federation of Allergy and Airways Diseases Patients' Associations (EFA), Brussels	patient	Netherlands	Co-author, patient representative
	Aszodi	Nora	Department of Dermatology, LMU Munich	clinical	Germany	Co-author
Prof. Dr.	Barbarot	Sebastien	University hospital, Nantes	primary prevention, education	France	Co-author
Prof. Dr.	Bieber	Thomas	Department of Dermatology and Allergy, University Hospital of Bonn	drug trials	Germany	Co-author
Dr.	Brough	Helen A.	Department of Pediatric Allergy, Division of Asthma, Allergy and Lung Biology, King's College London and Guy's and St. Thomas' NHS	paediatric allergy and clinical immunology	United Kingdom	Co-author

			Foundation Trust, London, United Kingdom			
Prof. Dr.	Calzavara Pinton	Piergiacomo	Dermatology Department, University of Brescia	phototherapy	Italy	Co-author
Dr.	Christen-Zäch	Stéphanie	University Hospital Lausanne	pediatric dermatology	Switzerland	Co-author
Dr.	Deleuran	Mette	Aarhus University Hospital	systemic treatments, immunodermatology	Denmark	Co-author
Dr. oec. troph.	Fink-Wagner	Antje-Henriette	Global Allergy and Airways diseases Patient Platform GAAPP, Vienna	patient representative	Germany	Co-author, patient represenative
Prof. Dr.	Flohr	Carsten	St John's Institute of Dermatology, King's College London	methodologist, clinical, systemic therapy	United Kingdom	Coordinator, co-author and methodologist (NMA)
Dr.	Fosse	Nicole	Department of Dermatology, University Hospital Basel	dermatology	Switzerland	Co-author
Dr.	Gáspár	Krisztián	Dept. of Dermatology and Dept. of Dermatological Allergology of the University of Debrecen	dermato-immunologist	Hungary	Co-author
Dr.	Gerbens	Louise	Amsterdam UMC (University Medical Centers), department of Dermatology	resident dermatology, PhD in atopic eczema, systemic therapy methodologist	Netherlands	Co-author
Prof. Dr.	Gieler	Uwe	Dept. Dermatology, Univ. Giessen	psychodermatology	Germany	Co-author
Prof. Dr.	Girolomoni	Giampiero	Dermatology and Venereology Section, Department of Medicine, University of Verona	immunobiology, treatments	Italy	Co-author
Prof. Dr.	Gregoriou	Stamatis	National and Kapodistrian University of Athens, Faculty of Medicine, Athens	Clinical	Greece	Co-author
Prof. Dr.	Moertz	Charlotte	Dept. of Dermatology and Allergy Centre, Odense University Hospital, University of Southern Denmark	clinical, dermatology, allergology	Denmark	Co-author
MD PhD	Nygaard	Uffe	Dept. of Dermato-Venerology, Aarhus University Hospital	immunobiology, Skin barrier, Biomarkers	Denmark	Co-author

	Redding	Magali	Eczema Outreach Support (UK)	Founding CEO of Eczema Outreach Support (UK), mother of a child with eczema	United Kingdom	Co-author, patient representative
MD, PhD	Rehbinder	Eva Maria	Dermatology Department, Oslo University Hospital	atopic dermatitis	Norway	Co-author
Prof. Dr. Dr.	Ring	Johannes	Dept Dermatology Allergology Biederstein, Technical University Munich	dermatology, immunology, allergy	Germany	Co-author
Dr.	Rossi	Mariateresa	Dermatology Unit Spedali Civili Hospital Brescia	phototherapy	Italy	Co-author
Dr.	Serra-Baldrich	Esther	Dermatology, Hospital of Sant Pau	clinical	Spain	Co-author
Prof. Dr.	Simon	Dagmar	Department of Dermatology, Inselspital, Bern University Hospital, University of Bern	clinical	Switzerland	Co-author
Prof. Dr.	Szalai	Zsuzsanna Zsófia	Pediatric dermatology unit, Heim Pál National Children's Institute Budapest	pediatric dermatology	Hungary	Co-author
Prof. Dr.	Szepietowski	Jacek C.	Department of Dermatology, Venereology and Allergology, Wroclaw Medical University	pruritus	Poland	Co-author
Dr.	Torrelo	Antonio	Hospital Infantil Niño Jesús, Madrid	pediatric dermatology	Spain	Co-author
Prof. Dr.	Werfel	Thomas	Hannover Medical School	Immunodermatology and allergology	Germany	Co-author
Prof. Dr.	Wollenberg	Andreas	Department of Dermatology, LMU Munich	clinical	Germany	Coordinator and co-author
	EuroGuiDem Team					
	Avila Valle	Gabriela	Division of Evidence Based Medicine (dEBM), Charité - Universitätsmedizin Berlin	systematic review methods	Germany	MD, Methodologist
	Dittmann	Martin	Division of Evidence Based Medicine (dEBM), Charité - Universitätsmedizin Berlin	information specialist	Germany	Team support, information specialist.
Dr.	Dressler	Corinna	Division of Evidence Based Medicine (dEBM), Charité - Universitätsmedizin Berlin	Systematic review methods	Germany	Methodologist, Deputy Lead EuroGuiDerm

Dr.	Kinberger	Maria	Division of Evidence Based Medicine (dEBM), Charité - Universitätsmedizin Berlin	Systematic review methods	Germany	MD, Methodologist
Prof. Dr.	Nast	Alexander	Division of Evidence Based Medicine (dEBM), Charité - Universitätsmedizin Berlin	Systematic review methods; certified guideline facilitator	Germany	MD, Methodologist: Director EuroGuiDerm

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

Topic	Name, Institution, Speciality
	[will be added later]

Declaration and management of conflicts of interest

We requested that experts declare their interests personally as described above through the online tool: ***Declaration of Interests for EuroGuiDerm Guidelines*** (http://ask.debm.de/index.php/981542?lang=en).

In line with the EuroGuiDerm Methods Manual, all experts can take part in the discussion. However, declaring personal-financial interests means that the person is not eligible to vote on recommendations. Of the 29 members of the guideline development group (GDG), 41.3 % (n=12) reported having personal-financial interests, see Table 2. 58.6% (n=17) of members reported having no personal-financial interests. Experts who had declared to have personal-financial COIs were not allowed to vote on the recommendations for systemic treatment including those pertaining to pregnancy.

TABLE 2: DECLARATIONS OF PERSONAL-FINANCIAL CONFLICTS OF INTERESTS AS PROVIDED BY EXPERT

Title	First name	Last name	As declared by the person:
Prof. Dr.	Sebastien	Barbarot	Dr Barbarot personal fees from Bioderma, Laboratoire La Roche Posay, Sanofi-Genzyme, AbbVie, Novartis, Janssen, Leo-Pharma, Pfizer, Lilly, UCB, Fresenius-Kabi, Samsung bioepis, Biogen
Prof. Dr.	Thomas	Bieber	T. Bieber is/has been lecturer and/or consultant for following companies: AbbVie, Allmiral, AnaptysBio, Arena, Asana Biosciences, Astellas, BioVerSys, Böhringer-Ingelheim, Daichi-Sankyo, Davos Biosciences, Dermavant/Roivant, DS Pharma, Evaxion, FLX Bio, Galapagos/MorphoSys, Galderma, Glenmark, GSK, Incytes, Kymab, LEO, Lilly, L´Oréal, MenloTx, Novartis, Pfizer, Pierre Fabre, Sanofi/Regeneron, UCB
Dr.	Mette	Deleuran	Participation in advisory boards and/or speaker for Sanofi-Genzyme, Regeneron, Galapagos, Eli-Lilly, Pfizer, Leo-Pharma, Pierre Fabre Dermo-cosmetique, Almirall, and AbbVie
Prof. Dr.	Giampier	Girolomoni	Personal fee for attending advisory boards or as a speaker at sponsored meetings from Sanofi, Regeneron, Galderma, Almirall, Abbvie, Pfizer, Leo pharma, Novartis, Eli Lilly

MD PhD	Uffe	Nygaard	Recieved honorary from Sanofi Genzyme A/S for teaching and providing written patient information regarding AE.
Prof. Dr. Dr.	Johannes	Ring	Honoraria for lectures Abbvie, Allergika
MD PhD	Rehbinder	Eva Maria	Received honoraries for lectures from Sanofi Genzyme, Leo Pharma, Novartis, Norwegian Psoriasis and Eczema Association, Norwegian Asthma and Allergy Association[1]
Dr.	Serra-Baldrich	Esther	Honorary as speaker, consultant , boards, for Pfizer, Sanofi, Novartis, Lilly, Abbvie, Galderma, Leo
Prof. Dr.	Jacek C.	Szepietowski	Advisory Board Member of Leo Pharma Speaker for Leo Pharma and Sanofi-Genzyme Investigator for Regeneron, Pfizer
Dr.	Antonio	Torrelo	Lilly, Sanofi, Pierre Fabre, Pfizer, Abbvie - All advisory boards and/or lectures and/or clinical trials
Prof. Dr.	Thomas	Werfel	Advisor and Research Funding from companies currently active in AE Research: Sanofi, Lilly, Pfizer, LEO, Galderma
Prof. Dr	Andreas	Wollenberg	AbbVie, Lilly, Pierre Fabre, Sanofi, Galderma, L'Oreal, Leo, Novartis
[1] declared in September 2021			

Scoping and defining the purpose of the guideline

The EuroGuiDerm team (CD and GA) and the guideline coordinators (AW and CF) prepared a scoping document. The manuscript was sent to the EDF members and the EuroGuiDerm Board of Directors in April 2020 for commenting and approval, see Appendix 2.

This guideline is an update of the consensus-based European guideline for the treatment of atopic dermatitis published in 2018. The guideline coordinators (AW and CF) developed 14 key questions, taking into account topics encompassed in the previous guideline but also covering new areas, in particular novel systemic medications and the management of atopic eczema in special populations (e.g. children, adolescents and pregnancy), also taking into account specific circumstances (e.g. pruritus, concomitant allergic diseases and occupational aspects). All key questions were presented to the GDG during the first online conference on 27 April 2020 and all GDG members could modifiy key question(s) for their assigned topic(s)/chapter(s) if required. New key questions were developed for the following sections: avoidance strategies, paediatrics and occupational aspects, see Table 3.

TABLE 3: OVERVIEW OF KEY QUESTIONS, SYSTEMATIC REVIEWS & METHODS

	Topic	Key Question(s) (KQ)	Methods	Identified systematic reviews
Consensus-based recommenations	Patient´s perspective	What is the patient's or caregiver's perspective on living with AE? What are therefore the needs in terms of treatment and delivering care?	Narrative review	-
	General measures and avoidance strategies	Can the presence of pollen, animal dander, physical activity, prespiration, irritating clothing, psychological stress, pollution, tobacco provoke and elicit the development of skin symptoms in atopic patients? Can the avoidance of these above mentioned factors help to prevent the exacerbation of AE? Does the avoidance of AE triggers allow for longer remission periods or complete clearance of AE? Can individual prevention measures be identified in patient with AE?	Center of Evidence Based Dermatology (CEBD) screened for Cochrane review on house dust mite, pollen and animal dander on 19 March 2020; expanded on 01 July 2020 to include pollutants, tobacco smoke, sweat, clothing and stress; update of the search in MEDLINE (Ovid) for each of the identified systematic reviews.	"House dust mite reduction and avoidance measures for treating eczema." Nankervis et al. 2015 [1](Cochrane Review) "Air pollution and atopic eczema: Systematic review of findings from environmental epidemiological studies." Krämer & Behrendt. 2019 [2] "A systematic review of vigorous physical activity in eczema" Kim & Silverberg 2016 [3] "Fabric selection in atopic dermatitis: An evidence-based review." Jaros et al. 2020 [4] "The association between maternal stress and childhood eczema: a systematic review". Chan et al. 2018 [5] "Prenatal maternal psychosocial stress and offspring's asthma and allergic disease: A systematic review and meta-analysis". Flanigan et al. 2018 [6]
Consensus-based recommenations	Basic emollient treatment and bathing	What basic treatments are effective and safe and can be recommended in patients with AE?	CEBD screened up to 19 March 2020., update search run for both of the identified reviews in MEDLINE (Ovid) and Embase (Ovid).	"Emollients and moisturisers for eczema." van Zuuren et al. 2017 (Cochrane Review) [7] "Efficacy and safety of wet wrap therapy for patients with atopic dermatitis: a systematic review and meta-analysis" Gonzalez-Lopez et al. 2017 [8]

	Dietary intervention	Are diagnostic procedures for the elucidation of IgE-mediated food allergy (food specific IgE and/or SPT, diagnostic elimination diets and challenge tests) routinely recommended in AE patients with a history of food-induced immediate symptoms? Are diagnostic procedures for the elucidation of combined reactions to foods (immediate reactions plus food-induced eczema (food specific IgE and/or SPT, diagnostic elimination diets and challenge tests) recommended in AE patients with a history of food-induced symptoms including worsening of eczema? Are diagnostic procedures for the elucidation of food as a trigger factor of AE (food specific IgE and/or SPT, elimination diets and challenge tests) recommended in AE patients with a history or suspicion of food-induced eczema? Is a therapeutic elimination diet recommended after the individual diagnosis of food allergy for food–induced AE? Are general dietary interventions (e.g. supplements of vitamins, general avoidance of certain foods e.g. cow´s milk, gluten) recommended for the management of AE? Are probiotics recommended for the management of AE?	CEBD screened up to 19 March 2020; update search run for the identified review in MEDLINE (Ovid)and Embase (Ovid);	"Probiotics for treating eczema." Makrgeorgou et al 2018 (Cochrane Review) [9] "Oral evening primrose oil and borage oil for eczema." Bamford et al. 2013 (Cochrane Review) [10] "Dietary supplements for established atopic eczema." Bath-Hextall et al. 2012 (Cochrane Review) [11] "Dietary exclusions for established atopic eczema." Bath-Hextall et al. 2008 (Cochrane Review) [12]
	Topical anti-inflammatory therapy	What is the efficacy (improvement in short and long-term disease control) and safety of topical anti-inflammatory therapies of AE?	CEBD screened on 5 May 2020.	"Systematic review and meta-analysis comparing topical corticosteroids with vehicle/moisturizer in childhood atopic dermatitis." Fishbein et al. 2019 [13] "Efficacy and safety of topical calcineurin inhibitors for the treatment of atopic dermatitis: meta-analysis of randomized clinical trials" Abędź & Pawliczak. 2019 [14] "Crisaborole ointment, 2%, for treatment of patients with mild-to-moderate atopic dermatitis: Systematic literature review and network meta-analysis" Fahrbach et al. 2020 [15] "Topical tacrolimus for atopic dermatitis". Martins et al. 2015 (Cochrane review) [16]
Consensus-based recommenat	Phototherapy	What is the efficacy and safety of different photo(chemo)therapy modalities (e.g. NB-UVB, PUVA, UVA1) for AE patients?	CEBD screened up to 19 March 2020,	"Photo(chemo)therapy in the management of atopic dermatitis: an updated systematic review with implications for practice and research." Garritsen et al. 2014 [17]

	Anti-pruritic therapy	Are there specific treatment options alleviating itch in AE?	CEBD screened up to 19 March 2020.	"Oral H1 antihistamines as 'add-on' therapy to topical treatment for eczema" Matterne et al. 2019 (Cochrane Review) [18]
	Antimicrobial therapy	What is the effectiveness and safety of different antibacterial, antiviral and antifungal treatments for infectious complications and alongside standard and/or systemic therapy for maintenance treatment?	CEBD screened up to 19 March 2020.	"Interventions to reduce Staphylococcus aureus in the management of eczema." George et al. 2019 (Cochrane Review) [19] "The role of yeast in atopic dermatitis revisited: a critical appraisal." Tsakok et al. 2015 [20]
Evidence-based recommendations	Systemic immunosuppressive treatment Biologics JAK inhibitores	What is the efficacy (improvement in short and long-term disease control (signs and symptoms) as well as quality of life) and safety of conventional and novel systemic therapies for the treatment of AE? Would changing from one systemic treatment to another lead to benefit in disease control? Does combination therapy of systemic treatments lead to additional benefit in disease control and quality of life?	CEBD screened up to 19 March 2020. A living systematic review with network meta-analysis was included and EtD Frameworks were developed.	"Systemic immunomodulatory treatments for patients with atopic dermatitis: a systematic review and network meta-analysis." Drucker et al. 2020 [21] (living systematic review) *Evidence to decision frameworks were developed.*
Consensus-based recomme	Other systemic treatment	What is the effectiveness and safety of other systemic anti-inflammatory agents for AE?	CEBD screened e up to 19 March 2020.	"Leukotriene receptor antagonists for eczema" Ferguson et al. 2018 (Cochrane Review) [22]
Consensus-based	Allergen-specific immunotherapy	What is the effectiveness and safety of allergen-specific immunotherapy for AE patients?	CEBD screened up to 19 March 2020.	"Specific allergen immunotherapy for the treatment of atopic eczema." Tam et al. 2016 (Cochrane Review) [23]
	Complementary medicine	What is the effectiveness and safety of complementary therapies for AE patients?	CEBD screened up to 19 March 2020; results assessed with AMSTAR-2.	"Topical application of Chinese herbal medicine for atopic eczema: a systematic review with a meta-analysis." Gu et al. 2014 [24] "Chinese herbal medicine for atopic eczema" Gu et al. 2013 (Cochrane Review) [25] "Alpine climate treatment of atopic dermatitis: a systematic review." Fieten et al. 2015 [26] "The effectiveness and safety of acupuncture for patients with

				atopic eczema: a systematic review and meta-analysis." Jiao et al. 2019 [27] "Complementary and alternative medicine for treatment of atopic eczema in children under 14 years old: a systematic review and meta-analysis of randomized controlled trials." Lu et al. 2018 [28] "Effectiveness and safety of herbal medicine for atopic dermatitis: an overview of systematic reviews". Kwon et al 2020 [29]
Consensus-based recommenations	Psychosomatic counselling and educational interventions	What is the effectiveness of psychological and educational interventions for AE patients?	CEBD screened up to 5 May 2020, results assessed with AMSTAR-2.	"Psychological and educational interventions for atopic eczema in children." Ersser et al. 2014 (Cochrane Review) [30] "Psychological and educational interventions for Atopic Dermatitis in Adults: a Systematic Review and Meta-analysis". Hashimoto et al. 2017 [31] "Systematic review of self management interventions for people with eczema". Ridd et al. 2017 [32] "Efficacy of health education on treatment of children with atopic dermatitis: a meta-analysis of randomized controlled trials". Li et al. 2020 [33]
Consensus-based recommenations	NEW: Considerations for pregnancy, breastfeeding or planning to have a child	What are the key differences in the management of AE in pregnant or breastfeeding women and for adults planning to have a child?	No systematic reviews were screened in the CEBD website for the KQ. Authors carried out a topic specific search in PubMed and a recent European task force position paper was considered.	"European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period." Vestergaard et al. 2019 [34]

Evidence-based recommendations	NEW: Considerations for pediatric and adolescent patients	Do paediatric AE patients show important phenotypic and diagnostic differences? Are there any differences between paediatric/adolescent and adult AE patients with regard to: the use of basic emollient therapy and other aspects of skin? the use of topical anti-inflammatory therapy? the use of systemic anti-inflammatory therapy? the use of adjuvant supportive measures?	A living systematic review with network meta-analysis was included , EtD Frameworks for systemic treatments were developed	"Systemic Immunomodulatory Treatments for Patients With Atopic Dermatitis: A Systematic Review and Network Meta-analysis." Drucker et al. 2020 [21]
Consensus-based recommenations	NEW: Occupational aspects	What is the impact of AE on work life? Which risks do AE patients have when starting/during work life? How to counsel AE patients regarding work life?	No systematic reviews were screened for the KQ. Authors carried out a topic specific search in PubMed and did a narrative review of the evidence available.	“The impact of atopic dermatitis on work life - a systematic review.” Nørreslet et al. [35]

Search methods and results, evidence selection & critical appraisal of evidence

As part of the scoping exercise, we searched for excisting guidelines, which did not lead to the identification of high quality (AGREE 2 evaluation) guidelines more recent than the 2018 version suitable for adaption. We also developed the PICO framework for all key questions concerning systemic treatment, see Appendix 2. The living network meta-analysis (NMA), including GRADE assessments, on systemic immunomodulatory treatment for atopic eczema , which one of the guideline coordinators is leading on, was identified [21]. Since the aim is to create a living guidelines, this systematic review is the most suitable one to use as evidence base.

Hence, the chapters on conventional systemic drugs (azathioprine, ciclosporin, systemic glucocorticosteroids, and methotrexate), biologics (dupilumab) and JAK-inhibitors (baricitinib) as well as systemic treatment for pediatric and adolescent populations are evidence-based. For mycophenolate mofetil no randomized controlled trials could be identified

Based on the results by Drucker at al. [21] (2020, original publication), we developed Evidence to Decision (EtD) frameworks that enclosed the following information: population, intervention, comparison, main outcomes, setting, perspective, background, desirable and undesirable effects, certainty of evidence, balance of effects, values, resources required, cost-effectiveness, equity, acceptability and feasibility.

For the subsections on the importance of the issues, equity, acceptability and feasibility we conducted a narrative review, see Table 4.

TABLE 4: NARRATIVE REVIEW ON PATIENT/CARER NEEDS OR PREFERENCES

Key Question PICOS	*What are the relevant stakeholde'rs views, needs or preferences concerning atopic eczema management?*
Population	Adults and children (including their caretakers/families) with a clinical diagnosis of atopic dermatitis; carers; health care professionals
Context	Europe
Study design	SR, Qualitative research, surveys/questionnaire studies, discreet choice experiments, and similar
Source	Centre of Evidence Based Dermatology (CEBD) systematic lists [36]; MEDLINE
Search strategy for stakeholders preferences used in MEDLINE (Ovid) 17 March 2020	
1. ((patient$ or subject$ or child$ or stakeholder or adolesc$ or teenager) adj3 (need* or view* or prefer*)).ab,ti.	
2. ((patient$ or child$) adj3 (survey or questionnaire or discreet choice or interview*)).ab,ti.	
3. ((Psycho social or psycho$ social) adj3 (need* or view* or prefer* or educat$)).ab,ti.	
4. 1 or 2 or 3	
5. exp Dermatitis, Atopic/	
6. atopic dermatitis.ab,ti.	
7. atopic eczema.ti,ab.	
8. 5 or 6 or 7	
9. 4 and 8	
10. limit 9 to yr="2010 -Current	

Two EtD frameworks were developed on the following main questions: 1) What is the efficacy (improvement *short-term* disease control [signs and symptoms] as well as quality of life) and safety of conventional and novel systemic therapies for the treatment of AE? This includes the subgroup considerations: children and adolescents, and 2) What is the efficacy (improvement *long-term* disease control [signs and symptoms] as well as quality of life) and safety of conventional and novel systemic therapies for the treatment of AE?, see Evidence Report.

Identification of literature concerning the remaining chapters

All other chapters are consensus-based chapters. Nevertheless, the EuroGuiDerm Team supported authors groups by searching for existing systematic reviews. To do so, we used the resources made available by the Centre of Evidence Based Dermatology (CEBD) [36] . The CEBD systematically search for and map systematic reviews on atopic eczema by topics. Lists are updated monthly.

All listed reviews published since 2013 were screened in line with the key questions specified in each chapter. Our exclusion criteria were: Reviews lacking risk of bias assessment of the included studies, including mixed patient populations (e.g psoriasis and atopic eczema patients) and narrative reviews. Cochrane reviews and systematic reviews with GRADE assessments were preferred for their higher methodological quality. We provided the author groups with the identified publications, see Table 3.

Furthermore, to include the latest evidence in the different chapters, we updated the search of 11 selected systematic reviews and if needed, updated the search strategy (search date 30 June 2020). Author were provided with EndNote files.

Lastly, for nine systematic reviews identified on complementary medicine, psychosomatic counselling and educational interventions one methodologist assessed the quality of the reviews using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR-2) checklist.

More detailed information about the above mentioned steps, such as the AMSTAR 2 evaluation results, are available upon request (euroguiderm(at)debm.de).

Developing background texts

The guideline coordinators (AW and CF) suggested which members of the GDG could develop which section of the guideline. The allocation of work was discussed and finalized during the first online meeting, see Table 5. All author groups received a chapter template and any systematic review identified via the CEBD website and updated search results, where applicable (Table 3).

TABLE 5: DISTRIBUTION OF TASKS

Chapter(s)/topic(s)	Authors
Introduction	Andreas Wollenberg, Carsten Flohr
Methods	Corinna Dressler, Maria Kinberger and Carsten Flohr
AE management from a patient´s perspective	Antje-Henriette Fink-Wagner, Magali Redding and Bernd Arents
General measures and avoidance strategies	Eva Maria Rehbinder, Krisztián Gáspár and Thomas Werfel
Basic emollient treatment, Bathing	Eva Maria Rehbinder, Bernd Arents, Jacek Szepietowski and Johannes Ring

Dietary intervention	Charlotte Moertz, Helen Brough, Johannes Ring and Thomas Werfel,
Topical anti-inflammatory therapy	Nora Aszodi, Giampiero Girolomoni andThomas Bieber
Phototherapy	Louise Gerbens and Piergiacomo Calzavara-Pinton,
Anti-pruritic therapy	Esther Serra-Baldrich, Jacek Szepietowski and Uwe Gieler
Antimicrobial therapy	Eva Maria Rehbinder, Nicole Fosse, and Sebastién Barbarot,
Introduction to systemic therapies	Mette Deleuran and Andreas Wollenberg,
Immunosuppressive treatment (CyA, Streoids, MTX, AZA, MMF)	Dagmar Simon, Mariateresa Rossi and Uffe Nygaard
JAK Inhibitors	Carsten Flohr, Antonio Torello and Stamatis Gregoriou
Biologics	Mariateresa Rossi and Mette Deleuran
Other systemic treatment	Dagmar Simon, Piergiacomo Calzavara-Pinton and Stamatis Grigoriou,
Allergen-specific immunotherapy	Esther Serra-Baldrich, Mariateresa Rossi and Krisztián Gáspár ,
Complementary medicine	Charlotte Moertz, Esther Serra-Baldrich and Mariateresa Rossi,
Psychosomatic counselling	Zsuzsanna Zsófia Szalai, Stéphanie Christen-Zäch, Sebastién Barbarot and Uwe Gieler (Group chapter)
Educational interventions	
Considerations for pregnancy	Andreas Wollenberg and Sebastién Barbarot,
Considerations for pediatric and adolescent patients	Magali Redding, Stéphanie Christen-Zäch, Zsuzsanna Zsófia Szalai, Antonio Torrelo and Krisztián Gáspár,
Occupational aspects	Esther Serra-Baldrich, Louise Gerbens and Uffe Nygaard

The co-authors prepared a draft chapter(s) including recommendations, which was subsequently reviewed and commented on by the EuroGuiDerm team and by at least one of the coordinators. Thereafter the co-authors revised the drafts where appropriate.

Developing recommendations and the consensus process

In accordance with the EuroGuiDerm Manual, we used phrasing suggested by the GRADE Working Group to standardize the wording of all recommendations [37], Table 6. Recommendations and texts were discussed and voted upon until a majority of more than 50% agreed.

TABLE 6: WORDING OF RECOMMENDATIONS [38-41]

Strength	Wording	Symbols	Implications
Strong recommendation **for** the use of an intervention	'We **recommend** . . .'	↑↑	We believe that all or almost all informed people would make that choice. Clinicians will have to spend less time on the process of decision-making, and may devote that time to overcome barriers to implementation and adherence. In most clinical situations, the recommendation may be adopted as a policy.
Weak recommendation **for**	'We **suggest** . . .'	↑	We believe that most informed people would make that choice, but a substantial number would not. Clinicians and health care providers will need to

the use of an intervention			devote more time on the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making requires substantial debate.
No recommendation with respect to an intervention	'We **cannot make a recommendation** with respect to . . .'	**0**	At the moment, a recommendation in favour or against an intervention cannot be made due to certain reasons (e.g. no reliable evidence data available, conflicting outcomes, etc.)
Weak recommendation **against** the use of an intervention	'We **suggest against** . . .'	↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
Strong recommendation **against** the use of an intervention	'We **recommend against** . . .'	↓↓	We believe that all or almost all informed people would make a choice against that intervention. This recommendation can be adopted as a policy in most clinical situations.

Online pre-voting

Between November 2020 and June 2021, a total of 8 online pre-votings took place to (a) familiarise the group with all draft recommendations and the chapter texts, to (b) collect feedback from the entire group and (c) to collect a vote on the recommendations. For the online pre-voting we used the tool LimeSurvey. While completing the survey, the answers and comments of the others were not visible to those working through the survey.

Each chapter was presented to all members of the guideline development group. Each member had the opportunity to agree or disagree with the draft text. In case of disagreement, the experts had the opportunity to comment or to suggest changes. All comments were reviewed by the two coordinators and all feedback was sent to the entire group.

The GDG members also voted on the draft recommendations and were specifically asked whether they agree or disagree with the strength and the wording of the recommendation(s). In case of disagreement, again, alternative suggestions and comments could be submitted. All members of the GDG were eligible to vote regardless of whether they declared any personal-financial interest. However, when calculating the strength of consensus on any recommendation pertaining to systemic treatment, we did not take the votes of those with person-financial interests into account. Although the EuroGuiDerm team could see how each person voted on the recommendations, this was never shared with the GDG. Submitted comments and suggestions were shared with the group. These were not anonymised.

The results and feedback from the online survey were then presented to the experts in the consensus conferences. If the coordinators or the co-authors, who had developed the drafts, had adjusted the recommendations based on the survey results, the changes were presented to the experts transparently.

Consensus conferences

Four online consensus conferences took place on 8 December 2020, 18 March 2021, 20 May 2021 and 22 July 2021. Alexander Nast, certified guideline facilitator, managed the process.

We used the nominal group technique [42]: Alexander Nast first presented the anonymised results, comments and any suggested changes from the pre-voting survey.

He then opened the floor for discussion. Benefits, harms, processes and procedures were extensively discussed. After the discussion, the final voting took place. The experts could 'agree', 'disagree' or 'abstain' for each vote. If 100% agreement was achieved in the prevoting and there was no need for further discussion, the result from the prevoting was adopted instead of another vote.

During the first session on 8 December 2020, the virtual 'hand raising' function was used for the voting. In each of the later sessions, we used the addin *Forms*. This allowed for anonymous voting. Experts who had declared personal financial interests were not allowed to vote on any recommendation pertaining to systemic treatment.

Upadacitinib was licensed after the last conference, hence we used the tool Limey survey to facilitate an online vote. 8 of 15 experts voted for strong recommendations, 6 for a weak recommendation and 1 was against including any recommendation.

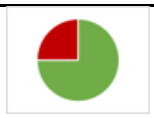
In the guideline itself, the strength of the consensus reached for each recommendation is reported as shown in Table 7.

TABLE 7: STRENGTH OF CONSENSUS

100 % consensus	100% agreement	
Strong consensus	Agreement of >95% - < 100% participants	
Consensus	Agreement of >75-95% participants	
Agreement of the majority	Agreement of >50-75% participants	

The recommendations are presented throughout this guideline as displayed below: alongside the wording of the recommendations the arrow(s) and color indicate the direction and the strength of each recommendation. The rate of agreement (consensus strength) is also displayed as the actual percentage and in form of a pie chart. For all systemic drugs, we added the standard dosages, separately for adults and children (European Medical Agency). Additionally, the certainty of evidence was added where applicable (bold – significant difference).

We **suggest** using azathioprine in AE patients who are candidates for systemic treatment.	↑	>75%

		 (15/16) Evidence and consensus based see EtD Framework

azathioprine: off licence; commonly used dosage

adults: 1-3 mg/kg per day

children: 1-3 mg/kg per day

Certainty of evidence:

Short term (8-16 weeks) vs placebo (NMA main analysis)

⊕⊕◯◯ LOW for mean difference / standardized mean difference **change in signs**, DLQI, Itch VAS, undesirable effects

Short term (8-16 weeks) vs placebo (NMA commonly used drugs)

⊕⊕◯◯ LOW for standardized mean difference **change in signs**, QoL

⊕◯◯◯ VERY LOW for standardized mean difference change in itch

For azathioprine versus other drugs, see Evidence Report

For each recommendation that is evidence-based, we added the certainty of the evidence when compared to placebo (see also Figure 1).

High ⊕⊕⊕⊕: we are **very confident** that the true effect lies close to that of the estimate of the effect.
Medium ⊕⊕⊕◯: we are **moderately confident** in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low ⊕⊕◯◯: 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.

FIGURE 1: DEFINITIONS OF "CERTAINTY OF EVIDENCE" [43]

Internal and external review

[to be added after the review phase]

Dissemination and Implementation

To foster the implementation of the guideline into clinical practice, we developed visual aids (stepped care plans) and summary tables

We developed a dissemination and implementation plan, see Table 8.

Barriers and facilitators to implementation/application

Quality standards and monitoring indicators

Over the two years following the publication of the EuroGuiDerm guideline on EDF website we will assess:

- Number of accesses and/or downloads from the EDF website
- Number of countries which adopted the guideline (translated the guideline as is, without change of content) by European countries, regions and non-European countries
- Number of countries which adapted the guideline (used parts of the guideline, or some recommendations) by European countries, regions and non-European countries

Evaluation Methods

Monitoring and evaluation is to be done at the national level.

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

Patient-perspective and needs

Two patient representatives and one parent representative from the Eczema Outreach Support were part of the GDG. All three representatives participated in the pre-votings and all consensus meetings; they had one vote each. The patient representatives developed a chapter on the patient's perspective, which is part of the main guideline. The other members of the group had no say in the content of this chapter.

In addition, we considered the available evidence on patient's and other stakeholder's needs, which we present as part of the evidence-to-decision framework (see Evidence Report).

Strength and Limitations

The GDG members – representing 12 countries - contributed a variety of issues to the discussions around, for example, about the availabilities of drugs, on local clinical practice and national guidelines.

We pursued a rigorous policy on conflicts of interests, which were all pre-declared. Over 50% of all GDG members did not have a CoI. Furthermore, experts with personal-financial interests were not allowed to vote on the recommendations for systemic treatment.

We used the living systematic review and network meta-analysis by Drucker et al. [21] as evidence base. The coordinator (CF) of the guideline is involved in the conduct of the review, where rigorous systematic methods were used. A protocol had been published[44]. We developed an evidence-to-decision framework for short term and long-term treatment, see Evidence Report.

Furthermore, we supported the co-authors, who developed the chapters other than those on systemic treatment, with systematic literature searches and focused screening, see Table 3.

For some chapters, such as the chapter on complementary medicine or on allergen specific immunotherapy, scarce evidence or only (very) low certainty evidence was available. For the complementary medicine chapter, we provided an AMSTAR 2 [45] assessment of the available systematic reviews.

Due to the numerous chapters of this guideline, we conducted eight online pre-voting survey, and four consensus conferences took place. Although this meant that the duration of the development of the guideline was significantly longer, all co-authors did work through every chapter one by one. There was enough time to thoroughly discuss each chapter and all recommendations.

We only conducted very little background research on cost and economic considerations when developing the evidence-to-decision frameworks. Due to the different health care systems and the local/national requirements, no further consideration was given to costs. Althoughe European Medical Agency centrally approves drugs in Europe, there may be specific restrictions to use that differ by country. Facilitators and barriers to implementation need to be considered locally. This European guideline is developed in a format that lends itself to local adoption or adaptation.

Update and Methods

The GDG will review the evidence summarized by Drucker et al. [21] every 18 months or when new treatments become available as part of a living EDF guideline on systemic therapies for atopic eczema.

The guideline subcommittee will also consider important clinical questions and review all consensus-based chapters every 5 years.

This process and updates will be available on the EDF website and communicated through appropriate channels.

TABLE 8: DISSEMINATION PLAN

Audience	Responsible Subcommittee member(s)	Communication and/or implementation tools to be used	Time at which they are to be developed, piloted or to take place	Is EuroGuiDerm support needed, and if yes what kind of support?
Dermatology, General Medicine, Patients / Patient Organisations, Research	A Wollenberg, C Flohr	Slide set (power point)	After external review	No
Dermatology, General Medicine, Patients / Patient Organisations, Research	EuroGuiDerm	Website	After external review	EuroGuiDerm Team to organize the website, layout etc
Dermatology, General Medicine, Research	A Wollenberg, C Flohr, EuroGuiDerm	Journal publication	Submission at the same time as the external review	Assistance with submission process
Dermatology, General Medicine, Patients / Patient Organisations, Research	EuroGuiDerm Team	Twitter, EuroGuiDerm newsletter	Once the website is running, each time the publication is early online	EuroGuiDerm Team

References

[1] Nankervis H, Pynn EV, Boyle RJ, Rushton L, Williams HC, Hewson DM, et al. House dust mite reduction and avoidance measures for treating eczema. *Cochrane Database Syst Rev.* 2015;1; Cd008426.

[2] Kramer U, Behrendt H. [Air pollution and atopic eczema : Systematic review of findings from environmental epidemiological studies]. *Hautarzt.* 2019;70; 169-184.

[3] Kim A, Silverberg JI. A systematic review of vigorous physical activity in eczema. *Br J Dermatol.* 2016;174; 660-662.

[4] Jaros J, Wilson C, Shi VY. Fabric Selection in Atopic Dermatitis: An Evidence-Based Review. *Am J Clin Dermatol.* 2020;21; 467-482.

[5] Chan CWH, Law BMH, Liu YH, Ambrocio ARB, Au N, Jiang M, et al. The Association between Maternal Stress and Childhood Eczema: A Systematic Review. *Int J Environ Res Public Health.* 2018;15.

[6] Flanigan C, Sheikh A, DunnGalvin A, Brew BK, Almqvist C, Nwaru BI. Prenatal maternal psychosocial stress and offspring's asthma and allergic disease: A systematic review and meta-analysis. *Clin Exp Allergy.* 2018;48; 403-414.

[7] van Zuuren EJ, Fedorowicz Z, Christensen R, Lavrijsen A, Arents BWM. Emollients and moisturisers for eczema. *Cochrane Database Syst Rev.* 2017;2; Cd012119.

[8] González-López G, Ceballos-Rodríguez RM, González-López JJ, Feito Rodríguez M, Herranz-Pinto P. Efficacy and safety of wet wrap therapy for patients with atopic dermatitis: a systematic review and meta-analysis. *Br J Dermatol.* 2017;177; 688-695.

[9] Makrgeorgou A, Leonardi-Bee J, Bath-Hextall FJ, Murrell DF, Tang ML, Roberts A, et al. Probiotics for treating eczema. *Cochrane Database Syst Rev.* 2018;11; Cd006135.

[10] Bamford JT, Ray S, Musekiwa A, van Gool C, Humphreys R, Ernst E. Oral evening primrose oil and borage oil for eczema. *Cochrane Database Syst Rev.* 2013; Cd004416.

[11] Bath-Hextall FJ, Jenkinson C, Humphreys R, Williams HC. Dietary supplements for established atopic eczema. *Cochrane Database Syst Rev.* 2012; Cd005205.

[12] Bath-Hextall F, Delamere FM, Williams HC. Dietary exclusions for established atopic eczema. *Cochrane Database Syst Rev.* 2008;2008; Cd005203.

[13] Fishbein AB, Mueller K, Lor J, Smith P, Paller AS, Kaat A. Systematic Review and Meta-analysis Comparing Topical Corticosteroids With Vehicle/Moisturizer in Childhood Atopic Dermatitis. *J Pediatr Nurs.* 2019;47; 36-43.

[14] Abędź N, Pawliczak R. Efficacy and safety of topical calcineurin inhibitors for the treatment of atopic dermatitis: meta-analysis of randomized clinical trials. *Postepy dermatologii i alergologii.* 2019;36; 752-759.

[15] Fahrbach K, Tarpey J, Washington EB, Hughes R, Thom H, Neary MP, et al. Crisaborole Ointment, 2%, for Treatment of Patients with Mild-to-Moderate Atopic Dermatitis: Systematic Literature Review and Network Meta-Analysis. *Dermatol Ther (Heidelb).* 2020;10; 681-694.

[16] Cury Martins J, Martins C, Aoki V, Gois AF, Ishii HA, da Silva EM. Topical tacrolimus for atopic dermatitis. *Cochrane Database Syst Rev.* 2015;2015; Cd009864.

[17] Garritsen FM, Brouwer MW, Limpens J, Spuls PI. Photo(chemo)therapy in the management of atopic dermatitis: an updated systematic review with implications for practice and research. *Br J Dermatol.* 2014;170; 501-513.

[18] Matterne U, Böhmer MM, Weisshaar E, Jupiter A, Carter B, Apfelbacher CJ. Oral H1 antihistamines as 'add-on' therapy to topical treatment for eczema. *Cochrane Database Syst Rev.* 2019;1; Cd012167.

[19] George SM, Karanovic S, Harrison DA, Rani A, Birnie AJ, Bath-Hextall FJ, et al. Interventions to reduce Staphylococcus aureus in the management of eczema. *Cochrane Database Syst Rev.* 2019;2019.

[20] Tsakok T, Schulenburg H, Smith C, Till S, Flohr C. The Role of Yeast in Atopic Dermatitis Revisited: a Critical Appraisal. *Current Dermatology Reports.* 2015;4; 228-240.
[21] Drucker AM, Ellis AG, Bohdanowicz M, Mashayekhi S, Yiu ZZN, Rochwerg B, et al. Systemic Immunomodulatory Treatments for Patients With Atopic Dermatitis: A Systematic Review and Network Meta-analysis. *JAMA Dermatol.* 2020;156; 659-667.
[22] Ferguson L, Futamura M, Vakirlis E, Kojima R, Sasaki H, Roberts A, et al. Leukotriene receptor antagonists for eczema. *Cochrane Database Syst Rev.* 2018;10; Cd011224.
[23] Tam HH, Calderon MA, Manikam L, Nankervis H, Núñez IG, Williams HC, et al. Specific allergen immunotherapy for the treatment of atopic eczema: a Cochrane systematic review. *Allergy.* 2016;71; 1345-1356.
[24] Gu S, Yang AW, Li CG, Lu C, Xue CC. Topical application of Chinese herbal medicine for atopic eczema: a systematic review with a meta-analysis. *Dermatology.* 2014;228; 294-302.
[25] Gu S, Yang AW, Xue CC, Li CG, Pang C, Zhang W, et al. Chinese herbal medicine for atopic eczema. *Cochrane Database Syst Rev.* 2013; Cd008642.
[26] Fieten KB, Weststrate AC, van Zuuren EJ, Bruijnzeel-Koomen CA, Pasmans SG. Alpine climate treatment of atopic dermatitis: a systematic review. *Allergy.* 2015;70; 12-25.
[27] Jiao R, Yang Z, Wang Y, Zhou J, Zeng Y, Liu Z. The effectiveness and safety of acupuncture for patients with atopic eczema: a systematic review and meta-analysis. *Acupunct Med.* 2020;38; 3-14.
[28] Lu CL, Liu XH, Stub T, Kristoffersen AE, Liang SB, Wang X, et al. Complementary and alternative medicine for treatment of atopic eczema in children under 14 years old: a systematic review and meta-analysis of randomized controlled trials. *BMC Complement Altern Med.* 2018;18; 260.
[29] Kwon CY, Lee B, Kim S, Lee J, Park M, Kim N. Effectiveness and Safety of Herbal Medicine for Atopic Dermatitis: An Overview of Systematic Reviews. *Evid Based Complement Alternat Med.* 2020;2020; 4140692.
[30] Ersser SJ, Cowdell F, Latter S, Gardiner E, Flohr C, Thompson AR, et al. Psychological and educational interventions for atopic eczema in children. *Cochrane Database Syst Rev.* 2014; Cd004054.
[31] Hashimoto K, Ogawa Y, Takeshima N, Furukawa TA. Psychological and Educational Interventions for Atopic Dermatitis in Adults: A Systematic Review and Meta-Analysis. *Behaviour Change.* 2017;34; 48-65.
[32] Ridd MJ, King AJL, Le Roux E, Waldecker A, Huntley AL. Systematic review of self-management interventions for people with eczema. *Br J Dermatol.* 2017;177; 719-734.
[33] Li Y, Han T, Li W, Li Y, Guo X, Zheng L. Efficacy of health education on treatment of children with atopic dermatitis: a meta-analysis of randomized controlled trials. *Arch Dermatol Res.* 2020;312; 685-695.
[34] Vestergaard C, Wollenberg A, Barbarot S, Christen-Zaech S, Deleuran M, Spuls P, et al. European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period. *J Eur Acad Dermatol Venereol.* 2019;33; 1644-1659.
[35] Nørreslet LB, Ebbehøj NE, Ellekilde Bonde JP, Thomsen SF, Agner T. The impact of atopic dermatitis on work life - a systematic review. *J Eur Acad Dermatol Venereol.* 2018;32; 23-38.
[36] Centre of Evidence Based Dermatology (CEBD). *Systematic reviews on eczema*. Available at: https://www.nottingham.ac.uk/research/groups/cebd/resources/eczema-systematic-reviews.aspx (last accessed 23 March 2020)
[37] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *Journal of clinical epidemiology.* 2011;64; 383-394.

[38] Guyatt GH, Oxman AD, Schunemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. *Journal of clinical epidemiology.* 2011;64; 380-382.
[39] The GRADE Working Group. 2018. Available at: http://www.gradeworkinggroup.org/ (last accessed July 10 2018)
[40] Werner RN, Nikkels AF, Marinovic B, Schafer M, Czarnecka-Operacz M, Agius AM, et al. European consensus-based (S2k) Guideline on the Management of Herpes Zoster - guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 1: Diagnosis. *J Eur Acad Dermatol Venereol.* 2017;31; 9-19.
[41] Werner RN, Nikkels AF, Marinovic B, Schafer M, Czarnecka-Operacz M, Agius AM, et al. European consensus-based (S2k) Guideline on the Management of Herpes Zoster - guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 2: Treatment. *J Eur Acad Dermatol Venereol.* 2017;31; 20-29.
[42] German Association of the Scientific Medical Societies (AWMF) - Standing Guidelines Commission. AWMF Guidance Manual and Rules for Guideline Development, 1st Edition 2012. English version. 2012.
[43] Schünemann H, Brożek J, Guyatt G, Oxman A. *Table 5.1 in GRADE handbook for Grading quality of evidence and strength of recommendations*. 2013. Available at: https://gdt.gradepro.org/app/handbook/handbook.html#h.9rdbelsnu4iy (last accessed 10.08.2021
[44] Drucker AM, Ellis A, Jabbar-Lopez Z, Yiu ZZN, Arents BWM, Burton T, et al. Systemic immunomodulatory treatments for atopic dermatitis: protocol for a systematic review with network meta-analysis. *BMJ Open.* 2018;8; e023061.
[45] Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ.* 2017;358; j4008.
[46] Harmonizing outcome measures for eczema (HOME). *Core outcomes for trials*. Available at: http://www.homeforeczema.org/research/index.aspx (last accessed 16 March 2020)
[47] Wollenberg A, Barbarot S, Bieber T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol.* 2018;32; 657-682.
[48] Wollenberg A, Barbarot S, Bieber T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. *J Eur Acad Dermatol Venereol.* 2018;32; 850-878.
[49] MoH (UA) - The State Expert Center MoH, Ukraine,,. Атопічний дерматит. Адаптована клінічна настанова, заснована на доказах [Atopic dermatitis. Adapted evidence-based guideline]. 2016.
[50] Lee JA, Choi J, Choi T-Y, Jun JH, Lee D, Roh S-S, et al. Clinical practice guidelines of Korean medicine on acupuncture and herbal medicine for atopic dermatitis: A GRADE approach. *European Journal of Integrative Medicine.* 2016;8; 854-860.
[51] C. C. Current Care Guidelines / the Finnish Medical Society Duodecim. *Atooppinen ekseema [Atopic eczema]*. 2016. Available at: https://www.kaypahoito.fi/hoi50077 (last accessed January 13 2020)
[52] Johnston GA, Exton LS, Mohd Mustapa MF, Slack JA, Coulson IH, English JS, et al. British Association of Dermatologists' guidelines for the management of contact dermatitis 2017. *Br J Dermatol.* 2017;176; 317-329.
[53] Werfel T. et al. AWMF - Association of Scientific Medical Societies. *Neurodermitis. S2e-LL (DDG)*. 2020. Available at: http://www.awmf.org/leitlinien/detail/ll/013-027.html (last accessed January 13 2020)

[54] Damiani G, Calzavara-Pinton P, Stingeni L, Hansel K, Cusano F, Pigatto PDM. Italian guidelines for therapy of atopic dermatitis-Adapted from consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis). *Dermatol Ther.* 2019;32; e13121.
[55] Katoh N, Ohya Y, Ikeda M, Ebihara T, Katayama I, Saeki H, et al. Clinical practice guidelines for the management of atopic dermatitis 2018. *J Dermatol.* 2019;46; 1053-1101.
[56] Rajagopalan M, De A, Godse K, Krupa Shankar DS, Zawar V, Sharma N, et al. Guidelines on Management of Atopic Dermatitis in India: An Evidence-Based Review and an Expert Consensus. *Indian journal of dermatology.* 2019;64; 166-181.
[57] Sidbury R, Kodama S. Atopic dermatitis guidelines: Diagnosis, systemic therapy, and adjunctive care. *Clin Dermatol.* 2018;36; 648-652.
[58] Wong ITY, Tsuyuki RT, Cresswell-Melville A, Doiron P, Drucker AM. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. *Can Pharm J (Ott).* 2017;150; 285-297.
[59] Katayama I, Aihara M, Ohya Y, Saeki H, Shimojo N, Shoji S, et al. Japanese guidelines for atopic dermatitis 2017. *Allergol Int.* 2017;66; 230-247.
[60] Nowicki R, Trzeciak M, Wilkowska A, Sokolowska-Wojdylo M, Lugowska-Umer H, Baranska-Rybak W, et al. Atopic dermatitis: current treatment guidelines. Statement of the experts of the Dermatological Section, Polish Society of Allergology, and the Allergology Section, Polish Society of Dermatology. *Postepy Dermatol Alergol.* 2015;32; 239-249.
[61] Werfel T, Heratizadeh A, Aberer W, Ahrens F, Augustin M, Biedermann T, et al. S2k-Leitlinie Neurodermitis [atopisches Ekzem; atopische Dermatitis] – Kurzversion. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft.* 2016;14; 92-106.
[62] National Institute for Health and Care Excellence (NICE). *Eczema overview*. Available at: https://pathways.nice.org.uk/pathways/eczema (last accessed 16 March 2020)
[63] LePoidevin LM, Lee DE, Shi VY. A comparison of international management guidelines for atopic dermatitis. *Pediatr Dermatol.* 2019;36; 36-65.
[64] Vermeulen FM, Gerbens LAA, Schmitt J, Deleuran M, Irvine AD, Logan K, et al. The European TREatment of ATopic eczema Taskforce (TREAT) Survey; prescribing practices in Europe for phototherapy and systemic therapy in moderate-to-severe adult atopic eczema patients. *Br J Dermatol.* 2020.
[65] Vestergaard C, Wollenberg A, Barbarot S, Christen-Zaech S, Deleuran M, Spuls P, et al. European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period. *Journal of the European Academy of Dermatology and Venereology.* 2019;33; 1644-1659.
[66] Drucker AM, Ellis A, Jabbar-Lopez Z, Yiu ZZN, Arents BWM, Burton T, et al. Systemic immunomodulatory treatments for atopic dermatitis: protocol for a systematic review with network meta-analysis. *BMJ Open.* 2018;8; e023061.
[67] Eckert L, Gupta S, Gadkari A, Mahajan P, Gelfand JM. Burden of illness in adults with atopic dermatitis: Analysis of National Health and Wellness Survey data from France, Germany, Italy, Spain, and the United Kingdom. *Journal of the American Academy of Dermatology.* 2019;81; 187-195.
[68] Wollenberg A, Oranje A, Deleuran M, Simon D, Szalai Z, Kunz B, et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. *J Eur Acad Dermatol Venereol.* 2016;30; 729-747.
[69] Gutknecht M, Reinert R, Augustin M. Review of health economic analyses in atopic dermatitis: how diverse is the literature? *Expert review of pharmacoeconomics & outcomes research.* 2019;19; 127-145.
[70] Ring J, Zink A, Arents BWM, Seitz IA, Mensing U, Schielein MC, et al. Atopic eczema: burden of disease and individual suffering - results from a large EU study in adults. *J Eur Acad Dermatol Venereol.* 2019;33; 1331-1340.

Appendices

APPENDIX 1: E-MAIL SEND TO FUNDING SOCIETIES

Dear xxx

We thank xxxx for the support of the EDF – EuroGuiDerm Guidelines Center. A broad base for the funding is crucial for the project's success. As one of the supporting societies, we want to invite you to suggest members for the guidelines groups.

The **EuroGuiDerm Atopic Dermatitis Guideline** is now being updated.

We are looking for

1. An established expert to become a member of the guideline development group, who ***preferably has little or no conflicts of interests with the pharmaceutical industry*** . We are looking for dermatologists with at least 10 years' experience as a consultant (or equivalent).

   and possibly

2. A junior doctor, who does ***not have any conflicts of interests with the pharmaceutical industry*** and who is interested in getting involved in guideline development work. Must have at least 4 years of clinical experience in dermatology.

The nominated experts will be involved in writing the background texts, draft recommendations and vote on the final guideline. Systematic search and literature approval will be done by the EuroGuiDerm center.

The deadline for nominations is January 15th, 2020. Please send your suggestions, and for the junior doctors please also a CV to atopic-dermatitis@debm.de .

Lastly, if there are any specific issues or key points arising nationally which should be taken into account during the guideline development, please inform us as soon as possible.

With best regards

Alexander

For more information on EuroGuiDerm, please visit our website:
https://www.edf.one/de/home/Guidelines/EDF---EuroGuiDerm.html

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APPENDIX 2: SCOPING DOCUMENT OF THE EUROGUIDERM ATOPIC DERMATITIS GUIDELINE – CREATED IN APRIL 2020

Update of the EuroGuiDerm Atopic Dermatitis (AD) guideline

SCOPING DOCUMENT

1. Planned methodological approach (guideline or consensus statement)

- EuroGuiDerm[a] Guideline on the systemic treatment for atopic dermatitis
- EuroGuiDerm Consensus Statement on topical therapy, phototherapy and other treatment options for AD

2. Broadly defined scope population/region/setting/interventions/comparisons/outcomes

- Population: Patients (all ages, all genders) with atopic dermatitis (AD; syn. atopic eczema) of all severities. Including special circumstances: pregnancy and concomitant allergic disease.
- Region: Europe
- Setting: Dermatologists and allergists in clinical practice
- Interventions/treatment approaches :
    - Systemic anti-inflammatory treatment (*Table 9*)
    - General measure and avoidance strategies
    - Basic emollient therapy and bathing
    - Dietary intervention
    - Topical anti-inflammatory treatment (including pro-active treatments)
    - Phototherapy
    - Antimicrobial therapy
    - Complementary medicine
    - Psychosomatic counselling
    - Educational interventions

Table 9: Systemic anti-inflammatory treatments*

Conventional immunosuppressants	TH2-blockers	Anti-IL 31	Small molecules	Other
Azathioprine	Dupilumab	Nemolizumab	Apremilast	Alitretinoin
Cyclosporine	Tralokinumab		Abrocitinib	Adriforant
Methotrexate	Lebrikizumab		Baricitinib	Corticosteroids (oral, IV, IM)

[a] The EDF has launched in 2018 the European Centre for Guidelines Development EuroGuiDerm in collaboration with Prof. Alexander Nast from the Division of Evidence-Based Medicine, Department of Dermatology, Charité University, Berlin. More information can be found on the EDF website: https://www.edf.one/home/Guidelines/Guideline-Methods-.html

Mycophenolate			Upadacitinib	

**Included are only those treatments deemed most relevant to clinical practice and those expected to get market authorization within the next ~ 1.5 years.*

- Comparisons: Direct, indirect and placebo.
- *Outcomes:* The Harmonising Outcome Measures for Eczema (HOME)[46] as well as the *European Dermatology Forum (EDF) atopic dermatitis guideline committee 2018*[47, 48] have both performed extensive exercises to determine essential outcomes in atopic dermatitis. It was deemed unnecessary to repeat this process for the update of the guideline.

  The core outcomes for AD in a trial setting (HOME)[b] or when it comes to the choice of therapy[47, 48] selected for the guideline update are:
  - Clinical signs: *Eczema Area and Severity Index (EASI);*
  - Overall disease severity as measured by the composite score *SCORing of Atopic Dermatitis (SCORAD) index;*
  - Patient-reported symptoms: *Patient-Oriented Eczema Measure (POEM);*
  - Quality of life: *Dermatology Life Quality Index (DLQI), Children's Dermatology Life Quality Index (CDLQI), Infant's Dermatitis Quality of Life Index (IDQOL).*

  Other outcomes selected additionally here:
  - Objective SCORAD *(o-SCORAD);*
  - Patient-oriented SCORAD *(PO-SCORAD);*
  - Investigator's Global Assessment *(IGA*, percentage of patients with IGA of 0 "clear" or 1 "almost clear") if no other objective score is reported;
  - Visual analogue scale itch *(VAS-itch);*
  - Typical adverse events: clinically relevant serious adverse effects of each systemic treatment, such as infection with all agents, conjunctivitis with the new biologic agents, renal function impairment and hypertension with cyclosporine, and gastrointestinal side effects with methotrexate.

3. Existing evidence and clinical guidance

This section provides a general overview of existing systematic review and guidelines.

[b] The other outcomes recommended by the HOME initiative were: NRS, RECAP and ADCT but these have only been recently recommended and validation studies are still ongoing and trials will not measure outcomes with these instruments yet.

Systematic reviews

The Centre for Evidence Based Dermatology (CEBD)[36] in Nottingham, United Kingdom, provides an overview of systematic reviews (monthly updates) since 2000, with the objective to inform clinicians about new guidelines and systematic reviews on atopic eczema. *Therefore, we did not perform a scoping search for systematic reviews. Depending on the final key questions chosen to be answered in the guideline, the CEBD lists will be used as a first resources for evidence.*

Guidelines

We conducted a non-exhaustive search[c] in the Guidelines International Network (G-I-N), National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), ECRI Guidelines Trust, Association of the Scientific Medical Societies (AWMF) and PubMed databases for existing guidelines published during the last 5 years, see appendix S1.

We identified 12 guidelines [49-60]: Seven of the 12 identified guidelines were from Europe [49, 51-54, 60, 61] (only one was published since the last update and is a local adaptation of the European guidelines [54]). Only two guidelines as well as the additional treatment updates of the NICE guideline for atopic dermatitis were evidence-based. Those three guidelines considered for adaptation are listed below, for the AGREE II evaluation (domain 3 only), see appendix S2.

- *"Clinical practice guidelines for the management of atopic dermatitis 2018." Japan* [55]
- *"Guidelines on Management of Atopic Dermatitis in India: An Evidence-Based Review and an Expert Consensus."*[56]
- *"Treating atopic eczema in children aged 12 and under and treating eczema in people over 12."*[62]

4. The purpose and objectives of guideline/ consensus statement

Background:

- New topical and systemic treatments for atopic dermatitis have been developed and approved.
- Several guidelines for the treatment of atopic dermatitis exist, but recommendations vary [63] and evidence-based recommendations for novel treatments are needed.
- Different prescribing practices between dermatologists across Europe and lack of experience in particular with systemic treatments have been reported [64]. There is therefore a need for current guidance and treatment algorithms on conventional and emerging therapies. Besides, expert

[c] *This is a general overview of what guidelines currently exist. Please do let us know if you know of any others.*

consensus advice on managing patients in special circumstances such as during pregnancy or, for example, with allergic comorbidities is essential [65].

- There is also a lack of clear guidance on switching patients from one systemic therapy to another and combined systemic therapy.

Objectives:

- To update the existing European AD treatment guideline.
- To generate recommendations and treatment algorithms on novel and established systemic treatments for atopic dermatitis based on the latest evidence.
- Provide guidance in the management of atopic dermatitis patients during pregnancy and AD patients with allergic comorbidities.
- Provide guidance on systemic drug switching and combination treatment.

5. Targeted users of guideline/consensus statement

- Dermatologists and allergists across Europe.

6. Connecting with relevant other organisations

- We are considering the evidence-based expert and non-expert opinion output of the HOME initiative (See above).
- We are considering the evidence-based expert opinion output of the European Task Force on Atopic Dermatitis (ETFAD). Members of the ETFAD are also in the guideline group, and we will make references to the work of the ETFAD where needed.
- Involvement of patients: patient representatives will be part of the guideline development group. A scoping review concerning patient needs will be conducted.
- A compressive, living systemic review and network meta-analysis (NMA) of systemic therapies is being published in late April 2020 [66] . Members of the NMA team are also in the guideline group.

7. Stakeholder recruitment

- National societies contributing financially to the EDF guidelines fund are contacted via email with a call for experts; those suggestions are priorities in the selection of experts to become members of the guideline development group (GDG).
- The guideline co-coordinators and the members of the EuroGuiDerm Board of Directors are also invited to suggest members.
- EDF members were invited to self-nominate twice via the EuroGuiDerm newsletter.

8. Other key issues

- Atopic dermatitis is associated with a high burden of disease in Europe [67], and there is a need for effective and long-term treatment for children and adults with atopic dermatitis [68].
- Economic evaluations based on interventions in children and adults are scarce. Resource usage and costs vary according to country and health care systems, making extrapolation from one setting to another difficult [69].
- Interventions for improving access to care, patient education and treatment adherence should be explored. Furthermore, patients' preferences should be taken into account [70].

9. Proposed key questions

Evidence-based questions:

(1) What is the efficacy (improvement in short and long-term disease control [signs and symptoms] as well as quality of life) and safety of conventional and novel systemic therapies for the treatment of AD? This question will be answered in three parts:

   i. Expert consensus for acute disease/flare control;
   ii. Evidence-based, 12-16 weeks;
   iii. Evidence-based, >16-52 week.

(2) Would changing from one systemic treatment to another lead to benefit in disease control?

(3) Does combination therapy of systemic treatments lead to additional benefit in disease control and quality of life?

The evidence-based sections will be based on a living systematic review lead by Carsten Flohr[66].

Consensus-based questions:

(4) What is the efficacy (improvement in short and long-term disease control) and safety of topical anti-inflammatory therapies of AD?

(5) What is the effectiveness and safety of different phototherapy regimen (e.g. NBUVB, PUVA, UVA1) for AD patients?

(6) What is the effectiveness of different therapeutic patient education regimen used for AD and does therapeutic patient education reduce the risk of patients experiencing side effects from topical and/or systemic treatments?

(7) What are the important provocation factors for AD (such as climate, allergen exposure (e.g. house dust mite, mould), skin irritants, food allergens, stress, water hardness), and how should patients avoid them?

(8) What is the optimal skin care regimen for AD patients, for instance regarding bathing (frequency, temperature, duration, bath additives (oils/emollients/bleach), emollient use afterwards yes/no), and showering?

(9) What is the effectiveness and safety of dietary exclusions or supplements for the treatment of AD?

(10) What is the effectiveness and safety of different antibacterial, antiviral and antifungal treatments for infectious complications and alongside topical and/or systemic therapy?

(11) What is the effectiveness and safety of complementary and alternative diagnostic and therapeutic procedures for AD patients?

(12) What is the effectiveness of psychological/psychosomatic/psychotherapeutic interventions for AD patients?

(13) What are key differences in the diagnosis and management of pediatric compared to adult AD (consider infants, children and adolescents separately).

(14) What are key differences in the management of AD in pregnant women?

SCOPING DOCUMENT - APPENDIX S1 SEARCH FOR EXISTING GUIDELINES

Search terms

atopic dermatit* OR atopic eczem* OR neurodermitis (in PubMed additionally with “guideline” in title)

Search date

13 January 2020 (PubMed search limited to years 2017 - 2020)

Title	Organisation(s)	Date	Country/Region	Sources	Comments
Атопічний дерматит. Адаптована клінічна настанова, заснована на доказах [Atopic dermatitis. Adapted evidence-based guideline][49]	MoH (UA) - The State Expert Center, Ministry of Health, Ukraine	Jul 04, 2016	Ukraine	G-I-N	language: Ukrainian
Evidence-Based Clinical Practice Guidelines for atopic dermatitis in Traditional Korean Medicine[50]	KIOM (KO) Korea Institute of Oriental Medicine	Jul 11, 2016	Republic of Korea	G-I-N	-
Atooppinen ekseema [Atopic eczema][51]	CC (FI) - Current Care Guidelines / the Finnish Medical Society Duodecim	Feb 03, 2009 (update 2016)	Finland	G-I-N	language: Finnish
Neurodermitis. S2e-LL (DDG) [Neurodermatitis][53]	AWMF (DE) - Association of Scientific Medical Societies	Mar 31, 2020	Germany	G-I-N	not evidence-based and is under review (not published)
British Association of Dermatologists' guidelines for the management of contact dermatitis 2017.[52]	British Association of Dermatologists (BAD)	Feb, 2017	United Kingdom	ECRI	guideline on contact dermatitis
Neurodermitis (S2k)[61]	AWMF (DE) - Association of Scientific Medical Societies	Mar, 2015	Germany	AWMF	language: German
Italian guidelines for therapy of atopic dermatitis-Adapted from consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis).[54]	SIDeMaST, ADOI, SIDAPA	Nov, 2019	Italy	PubMed	based on old EDF GL

Clinical practice guidelines for the management of atopic dermatitis 2018.[55]	Katoh et al.	Dec, 2019	Japan	PubMed	boxes w/ recommendations, use of evidence levels (old Oxford)
Guidelines on Management of Atopic Dermatitis in India: An Evidence-Based Review and an Expert Consensus.[56]	Rajagopalan et al.	May, 2019	India	PubMed	Key Qs in appendix, use of evidence levels (old Oxford)
Atopic dermatitis guidelines: Diagnosis, systemic therapy, and adjunctive care.[57]	Sidbury et al.	Sep, 2018	United States	PubMed	summary of 2014 AAD Guidelines
Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I.[47]	EDF	May, 2018	Europe	PubMed	old EDF GL
Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II.[48]	EDF	Jun, 2018	Europe	PubMed	old EDF GL
Guidelines for the management of atopic dermatitis (eczema) for pharmacists.[58]	Wong et al.	May, 2017	Canada	PubMed	-
Japanese guidelines for atopic dermatitis 2017.[59]	Katayama et al.	Apr, 2017	Japan	PubMed	-
Atopic dermatitis: current treatment guidelines. Statement of the experts of the Dermatological Section, Polish Society of Allergology, and the Allergology Section, Polish Society of Dermatology.[60]	Nowicki et al.	Aug, 2015	Poland	PubMed	-

SCOPING DOCUMENT - Appendix S2: AGREE II evaluation (domain 3 only) of guidelines potentially suitable for adapation

AGREE II-Domain 3: Rigour of development									
Guidelines	**7. Systematic methods were used to search for evidence.**	**8. The criteria for selecting the evidence are clearly described.**	**9. The strengths and limitations of the body of evidence are clearly described.**	**10. The methods for formulating the recommendations are clearly described.**	**11. The health benefits, side effects, and risks have been considered in formulating the recommendations.**	**12. There is an explicit link between the recommendations and the supporting evidence.**	**13. The guideline has been externally reviewed by experts prior to its publication.**	**14. A procedure for updating the guideline is provided.**	**Quality score (0%-100%)**
Clinical practice guidelines for the management of atopic dermatitis 2018 **Katoh et al. 2018**	PubMed, Japana Centra Vevuo Medicina, and Cochrane Library were searched for the relevant literature published by the end of December 2015. But complete search strategy not given	Designs of studies used as references for the determination of the evidence level. Old Oxford was used for level of evidence	The evidence level was an eventual judgment concerning the "quality of evidence" based on evidence concerning important outcomes reached as a consensus of the committee	Recommendations were comprehensively evaluated on the basis of the magnitude of benefits expected from the recommended treatments and balance between the benefits and harm or burdens that may be caused by the treatments in consideration of the evidence level, clinical experience, balance between benefits and harms, values, and wishes for treatment. No information given on how consesus was reached	In consideration of the evidence level, clinical experience, balance between benefits and harms, values, and wishes for treatment	Each recommendation is followed by a description graph and level of evidence	No information given	No information given	
Rating	2	2	2	2	3	3	1	1	17%
Guidelines on Management of Atopic Dermatitis in India: An Evidence-Based Review and an Expert Consensus **Rajagopalan et al. 2019**	An extensive literature search was done in MEDLINE, Google Scholar, Cochrane, and other resources. Articles published in the past 10 years were reviewed. But complete search strategy not given	Articles published in the past 10 years were reviewed and recommendations were graded based on the quality of evidence as per GRADE . For level of evidence and strengh of recomendation old oxford was used	Their discussions were based on literature from clinical research articles and also from their experience and acumen	The members gave their independent views on the preselected recommendations in agree and disagree scale with an Indian perspective. No information given on how consesus was reached.	Unclear if harms and benefits were taken into account for every recommendation. Harms are listed in some recommendation boxes and text.	Each recommendation is presented in a box with level of evidence and evidence is decribed in the text	No information given	No information given	
Rating	2	2	2	2	2	3	1	1	15%
NICE interactive flowchart: Treating Eczema in people aged 12 and under Treating eczema in people over 12 Last updated: 31 July 2018	For NICE guidelines review questions must be developed and literature searches are plannes and carried out. For clinical pathways sources for updates for treatment are listed some of them included the search strategy many updated on the clinical pathway are fom STA.	Each technology appraisal included as source had PICO and inclusion and eclusion criteria.	All evidence is appraised and biases also identified also cost are taken into account. Because this is a pathway it was dificult to identify the quality of evidence used for each recommendation.	Appraisal Committee bases its recommendations on the evidence presented, including statements from consultees and commentators and the views expressed by clinical specialists, commissioning experts and patient experts at the Committee meeting. The TSA included in the pathagws overlook of comments from stakeholders and experts.	The appraisal committee take into account impact of benefits and harms and also cost-effectiveness,but in the pathway only the recommendations are given. In the sources cited the complete information can be found.	All recommendations and it respective source is given, but no studies are cited in the text or EtD frameworks given, this can only be found checking the source.	Either NICE guidelines or TSA have to be checked by external stakeholders. This is give on a summary table with comments from each stakeholder and actions taken by the appraissal comittee.	No information given, but an update is plan for the Eczema treatment in people aged 12 and under guidelines. Also TSA provide dates for possible updates.	
Rating	5	7	6	5	6	5	7	6	81%