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CLINICAL TRIAL REPORT

A Clinical Investigation of the Performance and Safety of Epaderm®, an Emollient Cream

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Introduction: Emollients provide an occlusive barrier for dry and atopic skin, retain moisture, protect it from irritants, and form the basis of eczema treatment.

Methods and Analysis: A prospective interventional single arm study to evaluate the performance and safety of Epaderm® Cream, an emollient and cleanser containing 25% (w/w) paraffin and 5% (w/w) glycerine (thereafter, an emollient cream), in patients with dry skin conditions. The primary outcome measure was participant evaluation of skin moisturisation after treatment with an emollient cream for up to 4 weeks. Secondary outcome measures included: evaluation of skin softness using a questionnaire and of pruritus on a visual analogue scale (VAS); clinician assessment of xerosis using Overall Dry Skin (ODS) score and measurement of skin hydration using a non-invasive device (MoistureMeterEpiD, Delfin Technologies) at each visit. Sign test and Wilcoxon signed rank test were used to analyse changes from baseline.

Results: A total of 114 participants completed the study. 84.2% (80 out of 95) of participants or parents strongly agreed or agreed that the cream improved skin moisturisation at 4 weeks of treatment at the target area ($p<0.0001$). 86.3% of participants agreed that skin softness improved after 4 weeks ($p <0.0001$). ODS score improved from 2.1 (standard deviation (SD) 1.0) to 0.7 (SD 0.8) at 4 weeks. Skin hydration at the target area improved from 31.5 (SD 9.3) to 40.5 (SD 8.3) ($p<0.001$) at 4 weeks. Mean skin itchiness reduced from 38.0 (SD 25.4) to 17.7 (SD 19.8) at 4 weeks ($p<0.0001$). Ten (8.3%) adverse device events (ADEs) were reported.

Conclusion: The emollient cream was well tolerated and demonstrated significant improvements in patient-reported skin moisturisation and softness as well as in clinical measurement of xerosis and skin hydration across all age groups including infants. The emollient cream can be recommended for dry skin conditions including atopic dermatitis and psoriasis.

Keywords: emollient, Epaderm, dry skin, eczema, psoriasis, atopic dermatitis

Introduction and Objectives

In healthy skin, corneocytes and intercellular lipids (which form a lipid mixture of ceramides, fatty acids and cholesterol) make up the resilient lipid barrier which protects from the entry of pathogens, allergens and irritants and prevents water loss.[1–3] Loss of integrity of the skin's lipid barrier is a key factor in the development of dry skin conditions and the restoration of the barrier function is central in their management.[2] In dry skin conditions, the skin's barrier function may be impaired for a variety of reasons and there are several potential triggers for dry skin.[1] Similarly to the permeability barrier, the antimicrobial skin barrier function may be compromised in dry skin conditions, notably, in atopic

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dermatitis, which could lead to colonisation by *Staphylococcus aureus*.[4] Indeed, dry skin conditions have multiple causes, but common to many is the loss of skin barrier function often accompanied by genetic mutations, most commonly of the gene encoding filaggrin (FLG).[5]

There is a long history of the use of emollients as part of the management of dry skin conditions; they are available in various forms and aim to improve barrier function and to relieve dryness and pruritus.[2] Emollients are moisturising agents which soften, moisturise and hydrate the skin. They provide an occlusive barrier for dry and atopic skin, retain moisture and protect it from irritants. Emollient therapy forms the basis of eczema treatment and guidelines recommend frequent, liberal use.[6,7] Simple emollients form an occlusive layer of non-physiological lipid or oil, such as petrolatum or mineral oil, reducing water loss. Emollients may include additional ingredients such as humectants, physiological lipids and antipruritic agents. Humectants such as urea and glycerol attract and retain water in the skin. Physiological lipids such as ceramides, cholesterol and free fatty acids are believed to restore the intercellular lipid matrix.[8] It is important, however, for clinicians to consider the individual nature of different skin types when choosing appropriate treatment options.

Clinical studies of the performance and safety of emollients help clinicians to determine the most suitable option for patients with dry skin conditions including atopic dermatitis and psoriasis.

Aim and Outcome Measures

The aim of this study was to confirm the performance and safety of Epaderm® Cream, an emollient and cleanser containing 25% (w/w) paraffin and 5% (w/w) glycerine (thereafter, an emollient cream), in participants with dry skin conditions, including eczema, psoriasis and other dry skin conditions requiring treatment with emollient, when used as intended in daily practice.

Primary Outcome Measure

Participant evaluation of skin moisturisation (hydration) after treatment with the emollient cream up to 4 weeks, using a questionnaire.

Secondary Outcome Measures

- Participant evaluation of skin softness after treatment at 2 and 4 weeks
- Researcher assessment using "Overall Dry Skin" (ODS) score,[9] at 2 and 4 weeks
- Skin hydration using a non-invasive device, MoistureMeterEpiD, at 2 and 4 weeks
- Frequency and quantity of use of the emollient cream
- Comfort during treatment
- Time to onset of effect (moist and soft)
- Pruritus or skin itchiness using a visual analogue scale (VAS)
- Participant evaluation of overall effect
- Frequency of use of the emollient cream as a skin cleanser
- Concomitant and previous medication use and treatment
- Adverse Device Effects (ADEs)

Study Design

Prospective, observational, single-arm study of an Investigational Medical Device, the emollient cream, consisting of 25% (w/w) paraffin and 5% (w/w) glycerine, in participants ranging in age (infants (0 to 36 months old), children (3–18 years old), adults (>18 years old)).

Methods and Analysis

Study Setting

Secondary care in Poole Hospital National Health Service (NHS) Foundation Trust and Primary care in three NHS general practices in Bristol.

Participants

Participants with eczema, psoriasis or other dry skin conditions who were considered suitable for treatment with emollient cream by the investigator. Full inclusion and exclusion criteria and the study protocol are available in the public domain (ClinicalTrials.gov: US National Library of Medicine).[10]

Recruitment

Participants were recruited by invitation to potential participants with dry skin conditions (eczema, psoriasis) identified by EMISWeb (primary care Electronic Patient Records) searches or by opportunistic identification in general practice or hospital dermatology clinics between 01 April 2019 and 25 October 2019.

The purpose of the study was explained to all participants and informed, written consent was obtained from all participants or parents of participants.

Intervention

The emollient cream, consisting of 25% (w/w) paraffin and 5% (w/w) glycerine. Patients were given advice about the importance of frequent and liberal use, backed up with a patient information leaflet on sufficient and safe use of the emollient.

Participants were asked to agree to use the study emollient frequently (at least twice daily) and liberally as their only emollient and soap substitute for the 4-week study period but could stop treatment if they were dissatisfied with the study emollient.

The amount of emollient use was determined by asking how many 500g containers of emollient cream were used over the 2- and 4-week period.

Participants were free to use other treatments such as topical steroids as usual but not to use other emollients.

Schedule of Assessment

Data was collected for each participant over a 4-week treatment period, with a visit at baseline (visit 1, day 0), at 2 weeks (visit 2, day 14) and at 4 weeks (visit 3, day 28) treatment. An evaluable participant was a participant with a baseline visit and at least one follow-up visit. Collected data was entered into an electronic Case Report Form (eCRF) using Viedoc™.

Participants were instructed not to shower or put on the emollient cream before the follow-up visits.

Information was collected on age, sex and relevant medical history at the initial visit; at 2 weeks and 4 weeks, information was collected on concomitant relevant treatment, skin disease/condition and severity. A target affected area was chosen by the investigators as an area of skin representative of the participants'

Table 1 Demographics and Baseline Values (ITT)

Variable	0–36 Months Old (n=33)	3–18 Years Old (n=42)	>18 Years Old (n=41)	All Age Groups (n=116)*
Skin disease/condition				
Eczema/atopic dermatitis	30 (90.9%)	33 (78.6%)	25 (61.0%)	88 (75.9%)
Psoriasis	0 (0.0%)	2 (4.8%)	5 (12.2%)	7 (6.0%)
Other dry skin condition	3 (9.1%)	7 (16.7%)	11 (26.8%)	21 (18.1%)
Body region (multiple regions can be selected)				
Head/Neck	22 (66.7%)	18 (42.9%)	12 (29.3%)	52 (44.8%)
Trunk (including the genital area)	29 (87.9%)	26 (61.9%)	18 (43.9%)	73 (62.9%)
Upper extremities	29 (87.9%)	35 (83.3%)	24 (58.5%)	88 (75.9%)
Lower extremities (including the buttocks)	32 (97.0%)	36 (85.7%)	27 (65.9%)	95 (81.9%)
Severity of disease/condition				
Mild	19 (57.6%)	21 (50.0%)	13 (31.7%)	53 (45.7%)
Moderate	14 (42.4%)	18 (42.9%)	26 (63.4%)	58 (50.0%)
Severe	0 (0.0%)	3 (7.1%)	2 (4.9%)	5 (4.3%)
Type of relevant previous treatment				
Topical	31 (93.9%)	39 (92.9%)	40 (97.6%)	110 (94.8%)
Systemic	0 (0.0%)	1 (2.4%)	1 (2.4%)	2 (1.7%)
Photo therapy	0 (0.0%)	0 (0.0%)	2 (4.9%)	2 (1.7%)
None	2 (6.1%)	3 (7.1%)	1 (2.4%)	6 (5.2%)
Did the subject shower in the morning before the visit?				
No	29 (87.9%)	40 (95.2%)	19 (46.3%)	88 (75.9%)
Yes	4 (12.1%)	2 (4.8%)	22 (53.7%)	28 (24.1%)
Duration of disease in months	24.0 (0.0) 24 (24; 24) n=3	61.5 (41.0) 48 (12; 180) n=41	122.5 (166.0) 60 (12; 720) n=29	84.2 (112.6) 48 (12; 720) n=73

Notes: For categorical variables n (%) is presented. For continuous variables Mean (SD)/Median (Min; Max)/n= is presented. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

overall skin condition, ie, not the most or least affected area.

Clinician assessment of xerosis was carried out using ODS score following guidelines on the European Group on Efficacy Measurement of Cosmetics and Other Topical Products,[9] where absent skin dryness = 0; faint scaling = 1; small scales = 2; small and larger scales = 3; large scales = 4.

Skin hydration was assessed by clinicians using MoistureMeterEpiD (Delfin Technologies), a device which non-invasively measured local percentage water content (0% to 100%) in the epidermis. The device was placed on the target affected area and the percentage water content was shown on the display.

Participant evaluation of skin moisturisation and softness was assessed using 5-point questionnaires and participant evaluation of pruritus was assessed using a visual analogue scale (VAS). Data were also collected on the quantity and frequency of emollient applied and ADEs.

Statistical Methods

Sign test was used to analyse change from baseline in ordered categorical and dichotomous variables and Wilcoxon signed rank test for changes in continuous variables. Analyses were based on the intention-to-treat population and confirmed by the per protocol population. All tests were two-sided with a significance level of 0.05.

The sample size calculation was based on that the investigation was looking at performance of the emollient cream measured as improved moisturisation evaluated by the participant. Assuming a power of 80% and using a sign test, a total of approximately 40 participants were needed

Table 2 Primary Endpoint: Skin Moisturisation (ITT)

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group
Visit 2		n=31		n=40		n=38		n=109	
	Did you notice any improvement in the moisturisation of your or your child's skin after 2 weeks treatment of the target affected area?								
	Strongly agree	9 (29.0%)		9 (23.1%)		11 (29.7%)		29 (27.1%)	
	Agree	15 (48.4%)		20 (51.3%)		19 (51.4%)		54 (50.5%)	
	Neither agree, nor disagree	6 (19.4%)		4 (10.3%)		5 (13.5%)		15 (14.0%)	
	Disagree	1 (3.2%)		4 (10.3%)		0 (0.0%)		5 (4.7%)	
	Strongly disagree	0 (0.0%)	<0.0001	2 (5.1%)	<0.0001	2 (5.4%)	<0.0001	4 (3.7%)	<0.0001
Visit 3		n=27		n=35		n=39		n=101	
	Did you notice any improvement in the moisturisation of your or your child's skin after 4 weeks treatment of the target affected area?								
	Strongly agree	12 (46.2%)		11 (34.4%)		15 (40.5%)		38 (40.0%)	
	Agree	9 (34.6%)		17 (53.1%)		16 (43.2%)		42 (44.2%)	
	Neither agree, nor disagree	5 (19.2%)		3 (9.4%)		5 (13.5%)		13 (13.7%)	
	Disagree	0 (0.0%)	<0.0001	1 (3.1%)	<0.0001	1 (2.7%)	<0.0001	2 (2.1%)	<0.0001

Notes: For categorical variables n (%) is presented. For comparison within groups Sign test was used. Missing values for the total n is not included in tables. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

in each subgroup: infants (0–36 months), children (3–18 years) and adults (>18 years old).

Ethics

The investigation was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and applicable regulatory requirements.

The study received a favorable ethical opinion from the London Riverside Research Ethics Committee and the Health Research Authority (IRAS ID: 251156). ISO 14155:2011 was followed in addition to national regulations. The study was registered at the public database ClinicalTrials.gov Identifier: NCT03738163.

Participants were free to discontinue participation from the investigation at any time, and without prejudice to further treatment. Participants were categorised as lost to follow-up when the investigation staff had performed at least one documented attempt to reach the participant, after the baseline visit.

Results

Of the 121 enrolled participants, 114 completed the study; six withdrew before the second visit so follow-up data were not available for analysis; one participant withdrew later (all seven participants withdrew for non-device-related reasons). Primary outcome data were available for 107 and 95 participants at 2 weeks and 4 weeks, respectively.

Table 1 shows participant demographics and baseline diagnoses, distribution and severity. 33 (29%) were infants ≤36 months, 40 (35%) were children from 3 to 18 years and 41 (36%) were adults (>18 years). The majority (88; 76%) had a diagnosis of atopic dermatitis or eczema, 7 (6%) psoriasis and 21 (18%) had other dry skin conditions that the investigator considered to require emollient therapy.

82.2% and 88.4% of participants reported applying the emollient cream at least every day at 2 and 4 weeks, respectively. The most common frequency of application

Table 3 Secondary Endpoints: Skin Softness (ITT)

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group
Visit 2		n=31		n=40		n=38		n=109	
	Did you notice any improvement in the softness of your or your child's skin after 2 weeks treatment of the target affected area?								
	Strongly agree	11 (35.5%)	<0.0001	10 (25.6%)	<0.0001	8 (22.2%)	<0.0001	29 (27.4%)	<0.0001
	Agree	15 (48.4%)		21 (53.8%)		18 (50.0%)		54 (50.9%)	
	Neither agree, nor disagree	4 (12.9%)		3 (7.7%)		9 (25.0%)		16 (15.1%)	
	Disagree	1 (3.2%)		4 (10.3%)		0 (0.0%)		5 (4.7%)	
	Strongly disagree	0 (0.0%)		1 (2.6%)		1 (2.8%)		2 (1.9%)	
Visit 3		n=27		n=35		n=39		n=101	
	Did you notice any improvement in the softness of your or your child's skin after 4 weeks treatment of the target affected area?								
	Strongly agree	10 (38.5%)	<0.0001	11 (34.4%)	<0.0001	12 (32.4%)	<0.0001	33 (34.7%)	<0.0001
	Agree	12 (46.2%)		16 (50.0%)		21 (56.8%)		49 (51.6%)	
	Neither agree, nor disagree	3 (11.5%)		4 (12.5%)		4 (10.8%)		11 (11.6%)	
	Disagree	1 (3.8%)		1 (3.1%)		0 (0.0%)		2 (2.1%)	

Notes: For categorical variables n (%) is presented. For comparison within groups Sign test was used. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

was twice daily as reported by 58.9% of participants at 4 weeks. The emollient cream was used as a skin cleanser in 64.2% and 76.9% of all participants and children ≤3 years, respectively.

Primary Outcome

The primary outcome was the patient's or parent's self-reported evaluation of skin moisturisation at up to 4 weeks after using the emollient cream.

77.6% (83/107) and 84.2% (80/95) of participants strongly agreed or agreed that skin moisturisation had improved after 2 and 4 weeks of treatment at the target area and this was represented across all age groups (Table 2). This change from baseline was statistically significant for all participants as well as for each age group at 2 ($p<0.0001$) and 4 weeks ($p<0.0001$).

Secondary Outcomes

86.3% of participants strongly agreed or agreed that skin softness improved after 4 weeks of treatment located at the target affected area ($p<0.0001$) and this change was reported in all age groups ($p<0.0001$) (Table 3).

Clinician evaluation using ODS score changed from 2.1 (SD 1.0) to 1.2 (SD 1.1) and 0.7 (SD 0.8) at 2 and 4 weeks respectively ($p<0.0001$) (Table 4). Xerosis at the target affected area was evaluated by clinicians at the baseline visit and was evenly distributed between the following categories: faint scaling, faint roughness and dull appearance; small scales in combination with a few larger scales, slight roughness, whitish appearance; and small and larger scales uniformly distributed, definite roughness, slight redness and possibly few superficial cracks. A total of nine participants

Table 4 Secondary Endpoints: Overall Dry Skin Score (ITT)

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group
Baseline	Overall Dry Skin Score (ODS)	n=33 1.94 (0.90) 2 (0; 4) n=33		n=40 2.23 (1.03) 2 (0; 4) n=40		n=41 2.20 (0.95) 2 (1; 4) n=41		n=114 2.13 (0.96) 2 (0; 4) n=114	
Visit 2	Overall Dry Skin Score (ODS)	n=31 1.16 (1.21) 1 (0; 4) n=31		n=40 1.29 (1.11) 1 (0; 4) n=38		n=38 1.19 (0.95) 1 (0; 3) n=36		n=109 1.22 (1.08) 1 (0; 4) n=105	
	Change of Overall Dry Skin Score (ODS) from baseline	−0.742 (0.965) −1 (−3; 1) n=31	<0.0001	−0.921 (0.969) −1 (−4; 1) n=38	<0.0001	−0.889 (0.919) −1 (−3; 2) n=36	<0.0001	−0.857 (0.945) −1 (−4; 2) n=105	<0.0001
Visit 3	Overall Dry Skin Score (ODS)	n=27 0.480 (0.653) 0 (0; 2) n=25		n=35 1.000 (1.017) 1 (0; 3) n=30		n=39 0.553 (0.686) 0 (0; 2) n=38		n=101 0.677 (0.823) 0 (0; 3) n=93	
	Change of Overall Dry Skin Score (ODS) from baseline	−1.32 (0.85) −1 (−3; 1) n=25	<0.0001	−1.13 (0.97) −1 (−3; 1) n=30	<0.0001	−1.61 (0.79) −2 (−3; 1) n=38	<0.0001	−1.38 (0.88) −1 (−3; 1) n=93	<0.0001

Notes: For continuous variables Mean (SD)/Median (Min; Max)/n= is presented. For comparison within groups the Wilcoxon Signed Rank test was used. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

Table 5 Secondary Endpoints: Evaluation of Dry Skin/Xerosis (ITT)

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group
Baseline		n=33		n=40		n=41		n=114	
	How do you evaluate the dry skin/xerosis on the target affected area? (Please check all that apply)								
	Absent	1 (3.0%)		1 (2.5%)		0 (0.0%)		2 (1.8%)	
	Faint scaling, faint roughness and dull appearance	10 (30.3%)		9 (22.5%)		12 (29.3%)		31 (27.2%)	
	Small scales in combination with a few larger scales, slight roughness, whitish appearance	13 (39.4%)		15 (37.5%)		12 (29.3%)		40 (35.1%)	
	Small and larger scales uniformly distributed, definite roughness, slight redness and possibly few superficial cracks	8 (24.2%)		10 (25.0%)		14 (34.1%)		32 (28.1%)	
	Dominated by large scales, advanced roughness, redness present, eczematous changes and cracks	1 (3.0%)		5 (12.5%)		3 (7.3%)		9 (7.9%)	
Visit 2		n=31		n=40		n=38		n=109	
	How do you evaluate the dry skin/xerosis on the target affected area? (Please check all that apply)								
	Absent	12 (38.7%)		11 (28.9%)		8 (22.2%)		31 (29.5%)	
	Faint scaling, faint roughness and dull appearance	9 (29.0%)		12 (31.6%)		18 (50.0%)		39 (37.1%)	
	Small scales in combination with a few larger scales, slight roughness, whitish appearance	4 (12.9%)		9 (23.7%)		5 (13.9%)		18 (17.1%)	
	Small and larger scales uniformly distributed, definite roughness, slight redness and possibly few superficial cracks	5 (16.1%)		5 (13.2%)		5 (13.9%)		15 (14.3%)	
	Dominated by large scales, advanced roughness, redness present, eczematous changes and cracks	1 (3.2%)		1 (2.6%)		0 (0.0%)		2 (1.9%)	
	Change of the dry skin/xerosis from baseline								
	Improvement of the dry skin	21 (67.7%)	0.0009	27 (71.1%)	<0.0001	26 (72.2%)	<0.0001	74 (70.5%)	<0.0001
	Unchanged condition of the dry skin	6 (19.4%)		9 (23.7%)		9 (25.0%)		24 (22.9%)	
	Deterioration of the dry skin	4 (12.9%)		2 (5.3%)		1 (2.8%)		7 (6.7%)	

(*Continued*)

Table 5 (Continued).

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group	n (%)	p-value Within Group
Visit 3		n=27		n=35		n=39		n=101	
	How do you evaluate the dry skin/xerosis on the target affected area? (Please check all that apply)								
	Absent	15 (60.0%)		11 (36.7%)		21 (55.3%)		47 (50.5%)	
	Faint scaling, faint roughness and dull appearance	8 (32.0%)		12 (40.0%)		13 (34.2%)		33 (35.5%)	
	Small scales in combination with a few larger scales, slight roughness, whitish appearance	2 (8.0%)		3 (10.0%)		4 (10.5%)		9 (9.7%)	
	Small and larger scales uniformly distributed, definite roughness, slight redness and possibly few superficial cracks	0 (0.0%)		4 (13.3%)		0 (0.0%)		4 (4.3%)	
	Change of the dry skin/xerosis from baseline								
	Improvement of the dry skin	23 (92.0%)		21 (70.0%)		37 (97.4%)		81 (87.1%)	
	Unchanged condition of the dry skin	1 (4.0%)		8 (26.7%)		0 (0.0%)		9 (9.7%)	
	Deterioration of the dry skin	1 (4.0%)	<0.0001	1 (3.3%)	<0.0001	1 (2.6%)	<0.0001	3 (3.2%)	<0.0001

Notes: For categorical variables n (%) is presented. For comparison within groups Sign test was used. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

displayed dominating large scales, advanced roughness, redness, eczematous changes and cracks at the baseline visit. Improvement of scales or lesions occurred during the subsequent follow-up visits whereby the number of lesions decreased to 2 at week 2 and no lesions were present after 4 weeks of the emollient cream application. 29.5% (n=31) of the participants had no lesions at the second follow-up visit compared to 2% at baseline. Further skin improvement was confirmed by the absence of lesions in 50.5% (n=47) of all participants after 4 weeks of the emollient cream application (Table 5).

Skin hydration at the target area, measured using a Moisture Meter EpiD, improved from 31.5 (SD 9.3) to 38.6 (SD 11.2) ($p<0.001$) and 40.5 (SD 8.3) ($p<0.001$) at 2 and 4 weeks, respectively, in all participants. Similar statistically significant improvements were found in all three age groups (Table 6).

Mean skin itchiness measured on a 100-point VAS reduced from 38.0 (SD 25.4) to 25.1 (SD 23.4) ($p<0.0001$) and 17.7 (SD 19.8) ($p<0.0001$) in all participants at 2 and 4 weeks respectively (Table 7).

Participants were asked about the time to improvement of skin moisturisation or softness and 71.0% reported improvement within 2 weeks at visit 2% and 5.3% reported no improvement at all at visit 3.

The overall effect of the emollient cream was rated good to excellent in 83.2% of all participants and 88.5% of children ≤3 years.

90.9% of participants reported no further flares of their skin condition during the 4-week study period.

Ten ADEs were recorded in 10 participants (8.3% out of 121 enrolled participants); 3 in infants ≤3 years, 4 in children aged 3–18 years and 3 in the adult group. All ADEs were related to an inflammatory rash or

Table 6 Secondary Endpoints: Hydration Measurement of Target Affected Area (ITT)

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group
Baseline	Hydration measurement of target affected area (MoistureMeterEpiD)	n=33 33.7 (8.7) 36 (12; 46) n=33		n=40 29.9 (8.1) 32 (11; 46) n=39		n=41 31.2 (10.8) 31 (13; 60) n=41		n=114 31.5 (9.3) 33 (11; 60) n=113	
Visit 2	Hydration measurement of target affected area (MoistureMeterEpiD) Difference of hydration measurement of target affected area (MoistureMeterEpiD) from baseline	n=31 38.1 (7.6) 40 (15; 53) n=31 4.58 (7.31) 3 (−10; 26) n=31	0.0006	n=40 35.4 (10.1) 38 (0; 47) n=38 6.70 (6.93) 6 (−5; 20) n=37	<0.0001	n=38 42.7 (13.8) 44 (12; 66) n=34 11.5 (9.8) 10 (−13; 35) n=34	<0.0001	n=109 38.6 (11.2) 39 (0; 66) n=103 7.67 (8.54) 6 (−13; 35) n=102	<0.0001
Visit 3	Hydration measurement of target affected area (MoistureMeterEpiD) Difference of hydration measurement of target affected area (MoistureMeterEpiD) from baseline	n=27 40.0 (6.0) 40 (26; 52) n=25 6.04 (8.42) 4 (−5; 26) n=25	0.0023	n=35 38.0 (7.1) 38 (13; 54) n=28 7.18 (7.64) 6 (−9; 22) n=28	<0.0001	n=39 42.7 (9.8) 42 (15; 64) n=38 11.1 (9.4) 11 (−7; 35) n=38	<0.0001	n=101 40.5 (8.3) 40 (13; 64) n=91 8.48 (8.80) 9 (−9; 35) n=91	<0.0001

Notes: For continuous variables Mean (SD)/Median (Min; Max)/n= is presented. For comparison within groups the Wilcoxon Signed Rank test was used. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

hypersensitivity reaction. During the study, no serious adverse events (SAEs) in relation to the investigational device were reported. One device deficiency was reported where the participant did not attend the follow-up visits due to an intermittent rash which subsequently self-resolved.

Discussion

Clinicians have a large range of emollients to choose from when treating patients with dry skin conditions. It is not clear whether any emollients are superior to others. In their 2017 review, which included an evaluation of clinical studies ranging from those comparing an investigational product with a placebo to comparisons with no treatment, van Zuuren et al concluded that participants found investigational products to be more effective in reducing eczema and symptoms of itch compared to control. While most moisturisers showed some beneficial effects, there was generally no evidence that one moisturiser is superior to another.[11]

Hon et al (2018) reviewed current classes of emollients in the market and their clinical efficacy in atopic dermatitis. Clinical data included studies relating to plant-derived products (such as coconut oil and aloe vera), animal products (such as lanolin and horse oil) and emollients with special additives such as ceramides, ectoin or antimicrobial peptides. The authors emphasised an importance of an appropriate emollient for patients with atopic dermatitis which may significantly improve compliance with emollient treatment.[12]

In this study, the emollient cream was found to be well tolerated and showed improvements in patient-reported skin moisturisation and softness, clinical measurements

Table 7 Secondary Endpoints: Amount of Itching (ITT)

Follow-Up	Variable	0–36 Months Old (n=33)		3–18 Years Old (n=40)		>18 Years Old (n=41)		All Age Groups (n=114)*	
		Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group	Mean (SD) Median (Min; Max) n=	p-value Within Group
Baseline	On a scale of 0 to 100, with 0 meaning no itching and 100 meaning the worst itching you can imagine, how much itching in relation to your skin condition have you had?	n=33 36.2 (28.3) 38 (0; 90) n=33		n=40 39.2 (23.7) 34 (2; 89) n=40		n=41 38.3 (25.1) 37 (0; 98) n=41		n=114 38.0 (25.4) 34.5 (0; 98) n=114	
Visit 2	On a scale of 0 to 100, with 0 meaning no itching and 100 meaning the worst itching you can imagine, how much itching in relation to your skin condition have you had?	n=31 27.7 (27.4) 20 (0; 84) n=31		n=40 25.6 (25.2) 18 (0; 91) n=40		n=38 22.4 (17.1) 19.5 (0; 70) n=36		n=109 25.1 (23.4) 20 (0; 91) n=107	
	Change of itching from baseline	−6.00 (30.76) −1 (−77; 66) n=31	0.21	−13.6 (26.4) −14 (−72; 42) n=40	0.0022	−16.5 (22.2) −11.5 (−95; 19) n=36	<0.0001	−12.4 (26.6) −10 (−95; 66) n=107	<0.0001
Visit 3	On a scale of 0 to 100, with 0 meaning no itching and 100 meaning the worst itching you can imagine, how much itching in relation to your skin condition have you had?	n=27 17.4 (22.0) 7 (0; 70) n=26		n=35 20.0 (21.1) 13 (0; 80) n=32		n=39 15.9 (17.2) 9 (0; 65) n=38		n=101 17.7 (19.8) 10 (0; 80) n=96	
	Change of itching from baseline	−18.9 (25.3) −15 (−71; 30) n=26	0.0003	−19.3 (31.6) −23.5 (−80; 50) n=32	0.0014	−23.3 (23.9) −21 (−96; 21) n=38	<0.0001	−20.8 (26.9) −20.5 (−96; 50) n=96	<0.0001

Notes: For continuous variables Mean (SD)/Median (Min; Max)/n= is presented. For comparison within groups the Wilcoxon Signed Rank test was used. *Baseline data was collected for n=116 participants (ITT) whereas n=114 participants completed the study.

of xerosis and skin hydration in participants with dry skin conditions, including children and infants. Improvements were observed after 2 weeks of treatment. The participants' assessments of the strong positive effect of the emollient cream on their skin condition were confirmed by the subjective clinicians' evaluation and use of an objective tool, MoistureMeter EpiD.

The broad eligibility criteria allowed for "real world" data to be captured, representative of real life dermatological practice in both primary care and in a hospital setting.

This was a single arm study so outcomes could be a result of reversion to the mean. However, most participants were recruited by invitation because they had a record of a dry skin condition and there is no indication that many were experiencing flares of their condition at the time of assessment. It is possible that the clinical intervention to encourage frequent and liberal use of the cream may have had an important impact on the observed benefits of this treatment, although this should be standard practice in advising patients with dry skin conditions. Other specific study interventions such as the use of a MoistureMeter EpiD and the frequency of follow-up may have improved concordance with the treatment recommendations.

The study was carried out in one secondary care hospital and three urban general practices. It is possible that these study populations may not be representative of all populations, including patients from different socio-economic, educational and ethnic backgrounds. A relatively small number of participants were enrolled in the psoriasis cohort and it is possible that the performance of the cream may vary depending on the underlying skin condition.

Skin hydration and clinical assessment of xerosis were assessed on a single target area and these may have been different if measured on a more or lesser affected area.

Conclusions

The study showed that the emollient cream was well tolerated and demonstrated significant improvements in patient-reported skin moisturisation and softness as well as in clinical measurement of xerosis and skin hydration across all age groups, including infants, when applied liberally as often as required. Based on the data, the emollient cream can be recommended as part of the management regime of dry skin conditions including atopic dermatitis and psoriasis in children and adults.

Data Sharing Statement

The authors do not intend to share any individual deidentified participant data in this manuscript.

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