SMC2817

delgocitinib cream (Anzupgo®)

LEO Pharma

07 November 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

delgocitinib (Anzupgo®) is accepted for use within NHSScotland.

Indication under review: Treatment of moderate to severe chronic hand eczema (CHE) in adults for whom topical corticosteroids are inadequate or inappropriate.

In two phase III studies, delgocitinib significantly improved treatment success at 16 weeks, based on the Investigator's Global Assessment for Chronic Hand Eczema, in patients with moderate to severe CHE, compared with vehicle cream. In a third phase III trial, delgocitinib also led to a significantly greater reduction in the Hand Eczema Severity Index score than alitretinoin in patients with severe CHE at week 12.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Delgocitinib is a pan Janus kinase (JAK) inhibitor that targets all four members of the JAK family of enzymes consisting of JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2). Inhibition of the JAK signalling pathway by delgocitinib attenuates the signalling of several pro-inflammatory cytokines, downregulating the immune and inflammatory responses in cells of relevance to chronic hand eczema (CHE) pathology. (1)

A thin layer of delgocitinib cream is to be applied on the affected areas of the hands and wrists, twice daily, until the skin is clear or almost clear. Treatment should be restarted if symptoms return. It should be discontinued if there is no improvement after 12 weeks of continuous treatment. (1)

1.2. Disease background

Hand eczema is a common inflammatory skin condition affecting the hands and wrists. It is considered chronic if it lasts for more than 3 months or relapses twice or more per year. It negatively impacts the quality of life and daily life of patients, due to disabling symptoms like redness, fissures, itching, burning sensations and pain. CHE involves skin barrier dysfunction, immune dysregulation and an altered skin microbiome. It is driven by multiple inflammatory pathways. (2-4)

1.3. Treatment pathway and relevant comparators

First-line treatment involves topical corticosteroids (TCS) and emollients, but prolonged use of TCS can cause long-term skin damage. Tacrolimus ointment, a topical calcineurin inhibitor (TCI), may also be used for CHE; while it may work less well than steroids, it does not carry any risk of skin thinning.

Phototherapy is a treatment option for adults with CHE refractory to TCS; however long-term use of phototherapy may increase the risk of skin malignancy.

Alitretinoin is the only licensed systemic option for severe CHE unresponsive to potent TCS, its use is limited by teratogenicity. It is accepted for use within NHS Scotland (SMC ID: 538/09) in adults who have severe CHE that is unresponsive to treatment with potent TCS. Clinical experts consulted by the SMC have indicated that alitretinoin may also be used off-label in patients with moderate disease.

Other systemic options for patients who are refractory or with contra-indication to first- and second-line therapy options, although evidence for their efficacy might be limited, include: ciclosporin, azathioprine, methotrexate or acitretin for hyperkeratotic CHE. Oral corticosteroids may also be used short-term and repeated use should be avoided.

In most cases, treatment can help control the condition but does not cure it. (2-5)

The submitting company consider that the relevant comparators for delgocitinib are phototherapy (for moderate and severe CHE) and alitretinoin (for severe CHE only).

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of delgocitinib for the indication under review comes from the DELTA 1, DELTA 2 and DELTA FORCE studies. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies (2, 6-9)

Criteria	DELTA 1 and 2	DELTA FORCE
Study design	International, randomised, double-blind, 16-week phase III studies	International, randomised, assessor-blinded, 24-week phase III study
Eligible patients	Key inclusion criteria were: • Adult with a diagnosis of CHE • Recent documented history (within one year before screening) of inadequate response to treatment with TCS or for whom TCS are documented to be otherwise medically inadvisable	
	• Disease severity graded as moderate to severe at screening and baseline according to a modified IGA-CHE (that is a score of 3 or 4 within a 5-point scale: 0 [clear], 1 [almost clear], 2 [mild], 3 [moderate], and 4 [severe]) • HESD itch score (weekly average) of ≥4 points at baseline	• Disease severity graded as severe at screening and baseline according to IGA-CHE (that is a score of 4)
Treatments	Delgocitinib cream 20 mg/g or cream vehicle to be applied twice daily throughout the 16-week treatment period.	Topical administration of delgocitinib cream 20 mg/g, twice-daily until week 16 or oral administration of alitretinoin capsules 30 mg (with an option to reduce to 10 mg), once-daily until week 12. Treatment could be continued up to week 24 depending on clearance status and clinical benefit
	If rescue treatment was initiated to control intolerable CHE symptoms, treatment with investigational medicinal product was discontinued and not allowed to be re-started.	
Randomisation	Randomisation in a 2:1 ratio stratified by region (Europe or North America) and baseline IGA-CHE score (3 or 4).	Equal randomisation stratified by subtype (hyperkeratotic or non-hyperkeratotic) and region (North America or Europe).
Primary outcome	IGA-CHE treatment success at week 16 (that is a score of 0 or 1 with at least a 2-step improvement from baseline to week 16)	Change in HECSI score from baseline to week 12
Secondary outcomes	See tables 2.2 and 2.3 for selected key secondary outcomes	
Statistical analysis	Efficacy analyses were performed in the full analysis set population, which included all patients who underwent randomisation and were exposed to investigational medicinal product.	Efficacy analyses were performed in the full analysis set, which included all randomised participants.
	A hierarchical statistical testing strategy was applied for the primary and key secondary outcomes. Missing data were imputed with WOCF (continuous outcomes) or non-response (binary outcomes). Data after initiation of rescue treatments or permanent discontinuation of trial drug were treated as missing.	

Abbreviations: CHE, chronic hand eczema; HECSI, Hand Eczema Severity Index; HESD, Hand Eczema Symptom Diary; IGA-CHE, Investigator Global Assessment for chronic hand eczema; TCS, topical corticosteroids; WOCF, worst observation carried forward.

Statistically significant improvements were seen with delgocitinib over vehicle cream and alitretinoin for all primary and key secondary outcomes. (2, 6, 7) Results are detailed in tables 2.2 and 2.3.

Table 2.2 DELTA 1 and DELTA 2 primary and key secondary outcomes results (2, 6)

	DELTA 1			**DELTA 2**		
	delgocitinib cream (n=325)	**cream vehicle (n=162)**	**Estimated treatment difference (95% CI); p-value**	**delgocitinib cream (n=313)**	**cream vehicle (n=159)**	**Estimated treatment difference (95% CI); p-value**
Primary outcome						
Proportion of patients with IGA-CHE treatment success at week 16	20%	9.9%	**9.8**% (3.6 to 16); 0.006	29%	6.9%	**22%** (16 to 28); <0.001
Selected key secondary outcomes						
IGA-CHE treatment success at week 8	23%	10%	**12%** (5.7 to 19); 0.001	32%	9.4%	**23%** (16 to 30); <0.001
HECSI-90 at week 16	30%	12%	**17%** (10 to 24); <0.001	31%	8.8%	**22%** (15 to 29); <0.001
Percentage change in HECSI, week 16	-56.5	-21.2	**-35.2** (-46.7 to 23.8); <0.001	-58.9	-13.4	**-45.5** (-56.4 to -34.6); <0.001
HESD itch reduction ≥4 points, week 16	47% (n=323)	23% (n=161)	**24%** (15 to 33); <0.001	47% (n=309)	20% (n=156)	**27%** (19 to 36); <0.001
HESD pain reduction ≥4 points, week 16	49% (n=291)	28% (n=149)	**22%** (12 to 31); <0.001	49% (n=294)	23% (n=141)	**26%** (17 to 35); <0.001
HESD reduction ≥4 points, week 16	47% (n=309)	24% (n=156)	**23%** (14 to 32); <0.001	44% (n=308)	21% (n=153)	**24%** (15 to 32); <0.001
DLQI reduction ≥4 points, week 16	74% (n=305)	50% (n=148)	**24%** (15 to 34); <0.001	72% (n=299)	46% (n=153)	**26%** (17 to 36); <0.001
Change in DLQI, week 16	-7.6 (n=321)	-3.9 (n=158)	**-3.6** (-4.7 to -2.6); <0.001	-7.0 (n=310)	-3.1	**-3.9** (-5.0 to -2.8); <0.001

Data are % or least squares mean. Abbreviations: CI, confidence interval; DLQI, Dermatology Life Quality Index; HECSI, Hand Eczema Severity Index; HECSI-90, at least 90% improvement in HECSI score from baseline; HESD, Hand Eczema Symptom Diary; IGA-CHE, Investigator's Global Assessment for chronic hand eczema; IGA-CHE TS, IGA-CHE treatment success, i.e. an IGA-CHE score of 0 (clear) or 1 (almost clear) with a ≥2-step improvement from baseline.

Table 2.3 DELTA FORCE primary and key secondary outcomes results (7)

	delgocitinib cream (n=250)	alitretinoin (n=253)	Estimated treatment difference (95% CI); p-value
Primary outcome			
Change in HECSI score, week 12	–67.6 (3·4; n=249)	–51.5 (3.4; n=250)	**–16.1** (–23.3 to –8.9); <0.001
Selected key secondary outcomes			
HECSI-90 at week 12	39% (n=249)	26% (n=250)	**13%** (4.3 to 21); 0.003
IGA-CHE treatment success at week 12	27% (n=250)	17% (n=253)	**11%** (3.3 to 18); 0.004
Change in HESD itch score (weekly average) from baseline to week 12	–3.0 (0.2; n=238)	–2.4 (0.2; n=238)	**–0.7** (–1.1 to –0.2); 0.005
Change in HESD pain score (weekly average) from baseline to week 12	–2.9 (0.2; n=238)	–2.3 (0.2; n=238)	**–0.6** (–1.1 to –0.1); 0.018
Change in HECSI score from baseline to week 24	–69.6 (3.8; n=249)	–45.1 (3.8; n=250)	**–24.5** (–32.6 to –16.4); <0.001

Data are % or least squares mean (standard error). Abbreviations: CI, confidence interval; HECSI, Hand Eczema Severity Index; HECSI-90, at least 90% improvement in HECSI score from baseline; HESD, Hand Eczema Symptom Diary; IGA-CHE, Investigator's Global Assessment for chronic hand eczema; IGA-CHE TS, IGA-CHE treatment success, i.e. an IGA-CHE score of 0 (clear) or 1 (almost clear) with a ≥2-step improvement from baseline.

Open-label extension results from DELTA 3 (extension of DELTA 1 and 2) were reported up to a year (from parent study baseline). Patients were to be treated with delgocitinib cream 20 mg/g twice daily, only if they needed it, to control their CHE. Results, including from the proportions of patients with IGA-CHE score of 0 or 1, HECSI-75 or HECSI-90, suggest continued benefit over the longer timeframe, consistent with DELTA 1 and DELTA 2.(8)

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) outcomes included: the Dermatology Life Quality Index (DLQI) score, EQ-5D-5L and EuroQol visual analogue scale (EQ VAS).

In DELTA 1 and 2, at week 16, percentages of patients with at least 4-point reduction of DLQI score from baseline, as well as change from baseline to week 16 in DLQI score, were significantly higher in the delgocitinib cream groups compared with their corresponding cream vehicle groups. [(2)] Results have been detailed in the Table 2.2. The data suggest treatment with delgocitinib cream lead to greater increases (improvement) in EQ-5D-5L index from baseline to week 16 and in EQ VAS scores, compared with cream vehicle. (10, 11)

In DELTA FORCE, the area under the curve for the reduction from baseline in DLQI score was higher with delgocitinib cream than with alitretinoin at week 24. Results have been detailed in the Table 2.3. The data suggest treatment with delgocitinib cream lead to some greater increases (improvement) in EQ-5D-5L index and in EQ VAS scores from baseline to week 12 and 24, compared with alitretinoin.(12)

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

Bayesian network meta-analyses (NMAs) were conducted due to an absence of direct evidence that compared delgocitinib and phototherapy. The NMAs included seven studies to compare the efficacy and safety of three treatments: delgocitinib, psoralen-UVA (PUVA), and alitretinoin, in patients with moderate to severe CHE. The three efficacy outcomes assessed were the proportion of patients achieving clear or almost clear skin as indicated by Investigator Global Assessment of Chronic Hand Eczema or Physician Global Assessment clear (0) or almost clear [1] (IGA-CHE/PGA 0/1) assessed as either a binary response or cumulative response; or Hand Eczema Severity Index at least 90% improvement in HECSI score from baseline (HECSI-90); and discontinuation due to adverse events (AE). The economics model included IGA-CHE/PGA 0/1 outcomes, analysed separately for the moderate and severe CHE subpopulations.

Table 2.4: Summary of indirect treatment comparison

Criteria	Overview
Design	Bayesian network meta-analyses
Population	Patients with moderate to severe CHE, previously treated with topical corticosteroids.
Comparators	Delgocitinib, alitretinoin, vehicle cream/placebo and PUVA
Studies included	DELTA 1 and DELTA 2 (6), DELTA FORCE (12), Worm 2022(13), ALPHA 2024(14), BACH (15) and HANDEL (16)
Outcomes	Efficacy NMA outcomes included: • IGA-CHE/PGA 0/1 endpoint response (proportion of patients who had achieved a response at a specific timepoint) at timepoint corresponding to each study's primary outcome (that is week 12 or 16) and at week 12 • IGA-CHE/PGA 0/1 cumulative response (proportion of patients who had ever achieved a response throughout the assessment period) at the study's primary outcome timepoint (week 12 or 16), at week 12 • HECSI-90 at timepoint corresponding to each study's primary outcome (that is week 12 or 16) and at week 12 Safety NMA • Discontinuation due to AEs
Results	The fixed effects models, which were preferred by the submitting company, show: Efficacy NMA: The evidence suggests delgocitinib was likely to be superior in achieving clear or almost clear response as indicated by IGA-CHE/PGA 0/1 and HECSI-90, when compared with alitretinoin and PUVA. For all comparisons of delgocitinib versus each comparator, the median odds ratios obtained were all >1, with 95% credible intervals excluding one for all comparisons. SUCRA values also suggests delgocitinib cream was highly likely to be the most efficacious treatment in the networks. Safety NMA: The evidence suggests delgocitinib was less likely to be discontinued due to AEs than alitretinoin or PUVA. Using the random effects models, the central estimates remained similar; however, the 95% credible intervals were wider and included 1, indicating no clear evidence of a difference in efficacy compared with PUVA or alitretinoin.

Abbreviations: CHE, chronic hand eczema; HECSI, Hand Eczema Severity Index; IGA-CHE, Investigator Global Assessment for chronic hand eczema; PGA, Physician Global Assessment; PUVA, psoralen-UVA

3. Summary of Safety Evidence

In the DELTA 1 and 2 studies, respectively, any treatment-emergent AE was reported by 45% (147/325) and 46% (143/313) of patients in the delgocitinib groups and 51% (82/162) and 45% (71/159) in the cream vehicle groups and these were considered possibly or probably treatment-related in 3.7% and 7.0% in the delgocitinib groups, and 8.0% and 6.9% in the cream vehicle groups. In the delgocitinib and vehicle cream groups respectively, patients with a reported severe AE were 3.7% and 1.0% versus 3.1% and 2.5%, and patients discontinuing therapy due to an AE were 0.6% and 0.3% versus 3.7% and 3.1%. (6)

In the DELTA FORCE study, any treatment-emergent AE was reported by 49% (125/253) of patients in the delgocitinib cream group and 76% (188/247) in the alitretinoin group and these were probably or possibly treatment-related in 9.5% and 54% respectively. In the delgocitinib cream and alitretinoin groups respectively, patients reporting a severe AE were 1.6% versus 5.7%, and patients permanently discontinuing therapy due to an AE was 1.2% versus 10%. (7) The most common adverse reactions with delgocitinib were application site reactions (1.0% In the pool of three vehicle-controlled clinical studies (DELTA 1, DELTA 2 and vehicle-controlled Phase 2b study 1273). (1, 2)

Delgocitinib cream was generally well tolerated with no significant safety concerns observed in trials. However, long-term safety data and data in elderly patients are limited, and a potential risk of non-melanoma skin cancer at long-term use due to local immunosuppression cannot be excluded, warranting a safety warning in the Summary of Product Characteristics (SPC) and post-marketing monitoring. (2)

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Delgocitinib is the first medicine licensed for the treatment of moderate to severe CHE in adults for whom topical corticosteroids are inadequate or inappropriate.
- Delgocitinib demonstrated clinically relevant benefits compared to vehicle cream in moderate to severe CHE and to alitretinoin in severe CHE. This was supported by both clinician (investigator-rated severity and extent of CHE) and patient reported outcomes (patient-rated signs and symptoms and CHE-related quality of life). (2)

4.2. Key uncertainties

- There are no direct comparisons against certain treatment options used in practice, such as phototherapy; thus Bayesian NMAs were conducted. Results suggest that delgocitinib may be more effective than PUVA or alitretinoin. However, estimates are uncertain, as suggested by the wide credible intervals. This is due to selecting the fixed effects models (which may underestimate variability), limited data including in patients with moderate CHE, and clinical and methodological heterogeneity across studies (including in the outcome measures, CHE severity, approach to handling missing data, or permitted concomitant topical corticosteroids).
- While alitretinoin, licensed for severe CHE, was used as an active comparator in DELTA FORCE,

it was only administered as monotherapy and combination with TCS or phototherapy was not permitted; therefore, the comparator arm in this study may not fully reflect optimal real-world treatment. In addition, clinical experts consulted by SMC suggest that alitretinoin may also be used off-label in patients with moderate disease.

- Some other uncertainties relate to a risk of bias due to the partial blinding design in DELTA FORCE and the approach to the handling of missing data in all DELTA studies (although there is some reassurance from additional analyses using different methods).(2)
- Long-term data for delgocitinib remain limited. Controlled comparisons extend only to 16 or 24 weeks. Open-label extension data suggest generally consistent efficacy with prolonged as-needed treatment with delgocitinib. (8) However, open-label data are available up to about a year, which may not fully capture long-term safety and sustained efficacy (including relapse and retreatment after treatment discontinuation) for a chronic disease treatment.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that delgocitinib is a therapeutic advancement, addressing an unmet need as a safe and effective topical option that offers a novel mechanism of action.

4.4. Service implications

Clinical experts consulted by SMC considered that the introduction of this self-applied medicine may not impact on the patient and/or service delivery.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified Patient Groups.

- We received a patient group submission from the National Eczema Society, which is a registered charity.
- National Eczema Society has received 25% pharmaceutical company funding in the past two years, including from the submitting company.
- The intense itching and pain from CHE disrupt sleep, concentration and increases infection risk, while daily management - including multiple treatments, frequent bedding changes, places a heavy physical and emotional strain on patients and caregivers. It disrupts daily activities, work, mental health and particularly affects parents/carers and those in occupations requiring frequent hand washing or chemical exposure. It imposes economic burdens through sick days and reduced productivity.
- Current treatment options are limited and often not very effective; while topical corticosteroids are often prescribed, concerns over effectiveness and long-term safety underscore the need for more options. There are widespread patient concerns about the significant adverse effects of alitretinoin.
- Managing CHE is especially challenging for women of child-bearing age due to the need for treatment options without pregnancy related precautions. Diagnosing the condition can be

difficult in those with darker skin tones as signs such as redness may be less visible leading to underdiagnosis and treatment.

- Delgocitinib, a non-steroidal topical treatment targeting inflammation provides an effective topical treatment for CHE that may particularly benefit women of childbearing age and those without access to secondary care.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	10 years.
Population	Adults with moderate to severe CHE for whom TCS are inadequate or inappropriate.
Comparators	Alitretinoin for severe CHE and PUVA for moderate and severe CHE.
Model description	Patients receive treatment for a period of a fixed course of 12 weeks. During this period patients may achieve a full response in any 4-week cycle. In the absence of full response by 12 weeks, patients' response is assessed as either partial, low, or insufficient based on IGA-CHE classification. Following week 12, stopping rules are applied based on criteria specific to therapy. In the case of full response patients cease treatment. Patients with an insufficient response at week 12 (i.e., no improvement from baseline) discontinue the initial treatment. Patients with a low or partial response at week 12 continue their treatment (as-needed) up to week 24, during which time full response may be achieved leading to treatment cessation. Depending on the severity of a relapse, treatment may be reinitiated 'as needed'. The threshold severity at which patients are eligible to reinitiate treatment varies by comparator (delgocitinib may be restarted at the point of a loss of response (IGA-CHE ≥ 2, mild), alitretinoin and PUVA are only restarted at the point of a moderate or severe relapse (IGA-CHE ≥ 3 or IGA-CHE 4, moderate or severe). Though the maximum duration of retreatment is 24 weeks, there is no limit to the number of rounds of retreatment (which does not involve a 12-week assessment), a patient can receive following response and relapse. Patients who discontinue other than upon achievement of full response proceed to next-line treatment or BSC.
Clinical data	The NMAs described in Section 2.3 determined rates of full response. The base case employed separate analyses for 12-week response in moderate and severe CHE. Scenario analyses included NMA based on the DELTA primary endpoint (16 weeks) and 'cumulative' endpoints – response at any point during the period. Endpoints in studies varied between IGA-CHE and PGA with assumptions as to comparability. Few studies enrolled patients with moderate CHE, and the model assumes the relative treatment effects of delgocitinib and alitretinoin in DELTA FORCE and of alitretinoin and PUVA in ALPHA would be similar if evaluated among patients with moderate CHE. Fixed effects meta-analyses were employed in preference to random effects models, which the submitting company rejected on grounds of imprecision without any clear diagnostic basis for preferring one method over the other. At week 12, patients not yet in full response for delgocitinib and alitretinoin were distributed across three non-response health states based on clinical data from the DELTA studies. For alitretinoin, the distribution was based on clinical data from the DELTA FORCE study. Delgocitinib had both a higher probability of full-response and non-response outcomes

	weighted more to partial response than alitretinoin. For severe CHE, the distribution applied to PUVA non-responders was assumed to be the same as for alitretinoin; for moderate CHE the distribution was assumed to be the same as for delgocitinib. The incidence of AEs was reported by the submitting company to be low for both delgocitinib and alitretinoin.
Extrapolation	The model allows for late response based on cumulative incidence at the end of DELTA 3. This later response is applied equally across all comparators (i.e. no further treatment effect is assumed). The model also assigns similar rates of relapse and subsequent full response. Treatment may be discontinued by choice, or as a result of relapse in a proportion of patients. Higher likelihoods of discontinuation were applied for alitretinoin and PUVA based on a post hoc analysis of DELTA FORCE and an indirect comparison based on ALPHA, respectively. Relapse rates (for each severity of relapse) were modelled to be common across all medicines, with the exception of mild relapse, for which a greater risk was assigned for delgocitinib as in DELTA FORCE median time to IGA-CHE ≥ 2 among responders was shorter among patients treated with delgocitinib. The probability of achieving a full response with retreatment following a relapse of any severity was assumed to be the same for both delgocitinib and alitretinoin, though the submitting company suggests this may underestimate delgocitinib's effectiveness at this point based on DELTA FORCE. The same retreatment response rate was applied for PUVA. Based on a post-hoc analysis of DELTA FORCE fewer delgocitinib patients who continued treatment after week 12 as non-responders discontinued before week 24 than with alitretinoin. A simple indirect comparison was applied based on discontinuation in ALPHA to derive higher discontinuation rates for PUVA relative to both delgocitinib and alitretinoin.
Quality of life	The model employs utility values from the DELTA study (mapped EQ-5D-3L from 5L), based on a mixed model with repeated measures (MMRM) for change from baseline to week 16 (the endpoint in the DELTA studies). Utility values differed by level of response and use of active therapy. UK general population utility estimates reported by Hernandez Alava (2022) were used to estimate a multiplier for each health state, including baseline, and adjust utility estimates over time. Each score was modelled to be slightly lower for best supportive care. Severe CHE was modelled with separate but similar estimates.
Costs and resource use	Weekly usage of delgocitinib was derived from an MMRM regression on weekly consumption in DELTA 1 and DELTA 2 (and DELTA FORCE for severe CHE). Estimates were modelled according to response; scenario analyses employed alternative overall mean usages. Alitretinoin is dosed as a single capsule per day. PUVA was assumed to involve two sessions per week . Monitoring costs were included for alitretinoin for a proportion of people (i.e. women of childbearing age). Health state based costs consisted of a single GP and dermatologist visit per annum in full-response, but the latter were four per annum in partial, low, or insufficient response.
PAS	No Patient Access Scheme is in place

*Other data were also assessed but remain confidential.**

6.2. Results

Base case economic results for patients with moderate and severe CHE are presented in Tables 6.2.1 and 6.2.2 respectively.

Table 6.2.1: Base case analysis moderate CHE

Technologies	Total costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
Delgocitinib	8,257	5.82	-	-	-
PUVA	8,787	5.77	-531	0.051	Dominant

Abbreviations: CHE = chronic hand eczema; Incr. = incremental; ICER = incremental cost-effectiveness ratio; LYG = life years gained; PUVA = psoralen-UVA; QALY = quality-adjusted life-year.

Table 6.2.2: Base case analysis severe CHE

Technologies	Total costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
Delgocitinib	9,181	5.738	-	-	-
Alitretinoin	8,847	5.699	334	0.039	8,501
PUVA	9,783	5.688	-602	-0.050	Dominant

Abbreviations: CHE = chronic hand eczema; Incr. = incremental; ICER = incremental cost-effectiveness ratio; LYG = life years gained; PUVA = psoralen-UVA; QALY = quality-adjusted life-year.

Delgocitinib was dominant compared to PUVA in both the moderate and severe populations, meaning it was estimated as resulting in lower costs and better health outcomes for patients.

6.3. Sensitivity analyses

Areas of uncertainty in the economic modelling were explored in scenario analysis. A selection of scenario results are presented in Table 6.3.

Table 6.3: Scenario analyses

	Parameter	Base case	Scenario	Moderate CHE	Severe CHE	
				vs PUVA	vs alitretinoin	vs PUVA
	Base case			Dominant*	8,501	Dominant
1	Delgocitinib usage	Response dependent	Mean usage from all DELTA studies (value CiC)	Dominant	7,003	Dominant
2			Mean usage from DELTA 2 study – Lowest reported (value CiC)	Dominant	368	Dominant
3			Mean usage from DELTA FORCE study – Highest reported (value CiC)	Dominant	17,733	Dominant
4			As-needed initial	Dominant	8,229	Dominant
5	NMA results	12-week outcomes	Primary	Dominant	6,554	Dominant
6			Cumulative	Dominant	9,741	Dominant
7	Distribution non-responders at week 12	Patients not yet in full response distributed across non-response health states based on data from all DELTA	Equal (as delgocitinib)	Dominant	4,256	Dominant
8			ALPHA for alitretinoin & PUVA - NRI	N/A	9,693	Dominant
9			ALPHA for alitretinoin & PUVA - OC	N/A	4,500	Dominant

		studies for delgocitinib and DELTA FORCE for alitretinoin				
10	Relapse	Time to relapse from DELTA FORCE study. Equal relapse rates assumed between alitretinoin and PUVA	Delgocitinib informed by DELTA 3 study	Dominant	10,632	Dominant
11			Risk for alitretinoin & PUVA 50% of risk with Delgocitinib	Dominant	18,456	Dominant
12	Data source	Synthesis	DELTA FORCE data only	N/A	16,629	8,909

Abbreviations: CHE = chronic hand eczema; ICER = incremental cost-effectiveness ratio; N/A = not applicable; NRI = non-responder imputation; OC = observed cases; QALY = quality-adjusted life-year.

Notes:

* Dominant: The assessed medicine was estimated as having lower costs and greater health outcomes than the comparator.

6.4. Key strengths

- The model design appeared well suited to the decision-problem, reflecting the relapsing responding nature of treatment for CHE and treatment specific relapse-retreatment pathways.
- The DELTA programme provided a range of evidence to underpin the population of the model, supplemented where necessary by assumptions that appear generally reasonable.
- The submitting company was clear regarding uncertainties such as distinctions between IGA-CHE and PGA, its reliance on assumptions of constant relative effects across disease severities where indirect evidence in specific severities is limited, and the sensitivity of its analyses to alternative delgocitinib usage intensities.
- NMAs included comprehensive coverage of heterogeneity in clinical studies' endpoint definitions.
- Model inputs in relating to health-related quality of life appeared reasonable, as did resource use assumptions, and the analysis was little influenced by modelled health state cost-offsets.
- A thorough exploration of alternative scenarios was presented, including analysis versus alitretinoin based on the direct evidence of DELTA FORCE.

6.5. Key uncertainties

- As there were minimal modelled cost-offsets, the analysis was highly sensitive to the amount of delgocitinib cream used (see Scenarios 1 to 4, Table 6.3); the DELTA FORCE based analysis (Scenario 12) incorporated the higher usage in that study.
- As the submitting company acknowledged there is some uncertainty relating to the different endpoints in the clinical studies (DELTA 1-3, DELTA FORCE, ALPHA, BACH, and HANDEL),

informing the NMAs. Several had used the PGA scale rather than the more recent IGA-CHE. The company argued the latter has a more stringent criterion for full-response and that this may represent an artificial constraint on delgocitinib's relative effectiveness, but this is itself uncertain.

- There was also heterogeneity in the severity of CHE at baseline in the included studies. Few studies enrolled patients with moderate CHE, and analyses were conducted using data from patients with severe CHE in DELTA 1 and DELTA 2; other studies predominantly recruited patients with severe CHE. The submitting company acknowledged that the consequent assumption that the relative treatment effects of delgocitinib and alitretinoin in DELTA FORCE and of alitretinoin and PUVA in ALPHA would be similar if evaluated among patients with moderate CHE is key to the economic model.
- The model relied on relative effects based on fixed effects NMAs as the submitting company rejected random effects analyses due to the level of imprecision. While there was therefore some uncertainty as to the treatment effect, the central estimates from the random effects analysis were found to have little impact on the ICER.
- The analysis for the moderate CHE population compares delgocitinib with PUVA, a licensed comparator, but not with alitretinoin, which may have some off-label use. Evidence submitted by the company suggests that under plausible assumptions cost-effectiveness in this population may be broadly comparable with that in severe CHE.

7. Conclusion

After considering all the available evidence the Committee accepted delgocitinib for use in NHSScotland.

8. Guidelines and Protocols

Published guidelines relevant to the indication under review include:

- the 2022 Guidelines for diagnosis, prevention, and treatment of hand eczema by the European Society of Contact Dermatitis (ESCD) Guideline Development Group. (4)
- the 2017 British Association of Dermatologists' (BAD) guidelines for the management of contact dermatitis (5)
- the 2023 S2k guideline diagnosis, prevention, and therapy of hand eczema. (17)

9. Additional Information

9.1. Product availability date

1 March 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 60-gram tube (£)
Delgocitinib cream	**A thin layer is to be applied on the affected areas, twice daily, until the skin is clear or almost clear.**	**595**

Costs from BNF online on 11 August 2025.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 4,975 patients eligible for treatment with delgocitinib in year 1 and 4,993 patients in year 3. The estimated uptake rate was 5% in year 1 and 14% in year 3. This resulted in 249 patients estimated to receive treatment in year 1 rising to 699 patients in year 3. The gross medicines budget impact was estimated to be £507k in year 1 rising to £1.4m in year 3. As other medicines were assumed to be displaced the net medicines budget impact was estimated to be £52k in year 1 rising to £146k in year 3.

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This assessment is based on data submitted by the applicant company up to and including 17 October 2025.

*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.