5.03 DELGOCITINIB, 20 mg/g (2%) cream, Anzupgo®, LEO PHARMA Pty Ltd

1 Purpose of submission

1.1 The Category 1 submission requested a General Schedule, Authority Required (Written) listing for delgocitinib for the treatment of moderate to severe chronic hand eczema (CHE).

1.2 Listing was requested on the basis of a cost-utility approach vs standard of care (SoC), and a cost-minimisation approach vs the nominated supplementary comparator dupilumab. Table 1 summarises the components of the overall clinical claim addressed by the submission.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Adults (aged ≥18 years) with moderate to severe CHE who have had an inadequate response to, or for whom topical corticosteroids are not advisable.
Intervention	Delgocitinib 20 mg/g (2%) topical cream applied twice daily to clean and dry affected skin of the hands and wrists until the skin is clear or almost clear. Patients should avoid using other topical products immediately before and after application of delgocitinib. In the event of recurrence of the signs and symptoms of CHE (flares), twice daily treatment of the affected areas can be re-initiated as needed.
Comparator	Main: SoC (non-medicated emollient use alone; avoidance of known irritants and allergens) Supplementary: Dupilumab
Outcomes	Primary outcome • IGA – CHE TS at Week 16 Key secondary outcomes • HECSI-75 (at least 75% improvement) at Week 16 • HECSI-75 at Week 8 • HECSI-90 at Week 16 • IGA – CHE TS at Week 8 • IGA-CHE TS at Week 4 • Percentage change in HECSI score from baseline to Week 16 Safety Quality of Life • DLQI • EQ-5D-5L Patient Reported Outcomes • HEIS • HESD
Clinical claim	Delgocitinib 20 mg/g cream is superior to SoC in terms of efficacy and non-inferior to SoC in terms of safety. Delgocitinib 20 mg/g cream is non-inferior to dupilumab in terms of efficacy. No safety claims were made for delgocitinib 20 mg/g vs dupilumab.

Source: Table 1, p21 of the submission.
CHE = chronic hand eczema; DLQI = Dermatology Life Quality Index; EQ-5D-5L = EuroQoL 5 dimensions 5 levels; HECSI = Hand Eczema Severity Index; HECSI-75 = Hand Eczema Severity Index 75% improvement; HECSI-90 = Hand Eczema Severity Index 90% improvement; HEIS = Hand Eczema Impact Scale; HESD = Hand Eczema Symptom Diary; IGA – CHE TS = Investigator's global assessment - chronic hand eczema treatment success; SoC = Standard of Care.
Note: IGA-CHE TS was defined as an IGA-CHE score of 0 (clear) or 1 (almost clear) with ≥2-step improvement from baseline.

2 Background

Registration status

2.1 ***TGA status at time of PBAC consideration****:* Registered on 5 September 2025. The TGA indication for delgocitinib is for the treatment of moderate to severe CHE in adults for whom topical corticosteroids (TCS) are inadequate or inappropriate.

Previous PBAC consideration

2.2 This is the first submission for delgocitinib in any indication for PBAC consideration. If recommended, delgocitinib will be the first PBS-listed treatment specifically for CHE. The PBAC recommended the nominated supplementary comparator, dupilumab, for the treatment of patients aged 12 years and older with severe atopic dermatitis who

are inadequately controlled on topical therapies in March 2020 (paragraph 7.1, dupilumab, Public Summary Document [PSD], March 2020 PBAC Meeting).

3 Requested listing

MEDICINAL PRODUCT medicinal product pack	DPMQ	Max. qty packs	Max. qty units	No. of Rpts	Available brands
DELGOCITINIB					
Delgocitinib 20 mg / g (2%) cream 60 g 1 tube	Published: $[redacted]*	1	1	1	Anzupgo

* DPMQ updated using July 2025 mark-ups (DPMQ proposed in submission was $902.60)

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: ☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
Episodicity: Chronic
Severity: Moderate to severe
Condition: Chronic hand eczema
PBS indication: Chronic moderate to severe hand eczema / dermatitis
Treatment Phase: Initial and continuing
Restriction Level / Method: Authority Required Written
Treatment criteria: Must be treated by or in consultation with a dermatologist
Clinical criteria:
Patient must have moderate to severe hand eczema with an Investigator Global Assessment-Chronic Hand Eczema (IGA-CHE) score of 3 or 4;
AND
Patient must have moderate to severe hand eczema that lasts for more than 3 months at a time, or has returned twice or more within the last 12 months;
AND
Patient must have failed to achieve an adequate response to topical medium to high potency corticosteroids in the past 12 months;
OR
Use of topical corticosteroids is medically inadvisable for this patient;
AND
The treatment must be as monotherapy.
Population criteria:
Prescriber instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed CHE Authority Application – Supporting Information form which includes the following: (c) the completed current Investigator Global Assessment-Chronic Hand Eczema (IGA-CHE) calculation sheet including the date of assessment of the patient's condition
Administrative Advice: NOTE Moderate to severe chronic hand eczema is defined as IGA-CHE score of 3 or 4 NOTE Failure to achieve adequate response to topical medium to higher potency corticosteroids is defined as failure to achieve IGA-CHE score of ≤ 2 despite daily use. NOTE No increase in the maximum quantity or number of units may be authorised. NOTE No increase in the maximum number of repeats may be authorised.

3.1 The submission did not propose a Special Pricing Arrangement (SPA).

3.2 The proposed maximum quantity and number of repeats were considered appropriate. Across the DELTA 1-3 studies, the mean amount of cream used per week ranged from 7.47g (DELTA 3, weighted mean) to 8.54g (DELTA 1). Considering minor variation in use and some wastage, a 60 g tube was estimated to last approximately 6 weeks.

3.3 The submission proposed that delgocitinib be prescribed by specialist dermatologists to ensure appropriate management of moderate to severe disease in adults with inadequate response to, or unsuitable for, TCS. To support access in rural and remote areas, prescribing by other medical practitioners, such as GPs, under dermatologist guidance was also proposed. The PBAC considered that as there are known issues accessing dermatologists, and in recognition of delgocitinib as a topical therapy, that it would be reasonable for delgocitinib to be able to be prescribed by medical practitioners, including general practitioners, for the treatment of moderate to severe CHE.

3.4 The proposed restriction did not include a criterion limiting treatment to adults although the draft TGA Product Information (PI) indication referred specifically to adult patients and the pivotal trials excluded paediatric patients. Further, the economic and financial models in the submission did not include children and adolescents (<18 years).

3.5 The proposed restriction requires that patients have failed to achieve an adequate response to topical medium to high potency corticosteroids or for the use of topical corticosteroids to be inadvisable. The proposed restriction defined 'an inadequate response' as an Investigator Global Assessment – Chronic Hand Eczema (IGA-CHE) score of 3 or 4 within the previous 4 weeks. The IGA-CHE is a novel Clinician-reported outcome measure that assesses CHE severity using the clinical characteristics of erythema, scaling, lichenification/hyperkeratosis, vesiculation, oedema and fissures. The ESC noted that the submission did not provide a definition of 'inadvisable'.

3.6 The submission did not propose a separate restriction for the continuation phase. It stated that patients who completed a course of delgocitinib, responded, and later relapsed could access delgocitinib under the same restriction. The submission noted that patients with a full response would stop treatment and be classified as continuing patients. Those with a low or partial response could continue for up to 12 additional weeks; if they then responded, they would also become continuing patients; otherwise, treatment would cease. Non-responders would stop treatment and seek alternatives. Moreover, initial and relapsed patients differ, as initial treatment required failure to respond to medium- to high-potency TCS in the past 12 months, which may not apply to patients who previously responded and then relapsed. The pre-PBAC response stated that continuing patients would re-start treatment when signs and symptoms recur, without the need for another IGA-CHE assessment.

3.7 The submission did not propose a separate grandfathering restriction. The submission noted that fewer than 10 patients may require grandfathering at the time of the PBS listing of delgocitinib.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 CHE is a persistent inflammatory skin disorder mainly affecting the hands and wrists. It is defined by long-lasting or frequently recurring symptoms that involve skin barrier dysfunction, immune dysregulation, and alterations in the skin microbiome. The condition is driven by a combination of genetic and environmental factors. While many cases are triggered by exposure to irritants or allergens, approximately 20% have no identifiable cause[1]. Patients typically report itch and pain, both of which can significantly impact daily activities at home and work.

4.2 The submission stated that there are no Australian-based epidemiological studies specifically focused on hand eczema or CHE. The submission presented findings from the CHE epidemiology, Care, and Knowledge of real-life burden (CHECK) study[2], a large multinational observational study, which presented evidence from adult populations in 6 countries. It found that 62.7% of participants with physician-diagnosed CHE reported continuous symptoms for over 3 months and at least 2 flares within the past year. An additional 30.3% experienced 2 or more flares with symptoms lasting under 3 months, while 7.0% reported CHE lasting longer than 3 months with only 1 flare. The annual prevalence rate of CHE was reported to be 4.7%.

4.3 Hand eczema can be classified into aetiological (exogenous and endogenous) subtypes and clinical subtypes as described in the European Society for Contact Dermatitis (ESCD) guidelines[3]. Exogenous causes arise from external factors: allergic contact dermatitis from delayed hypersensitivity to allergens such as metals, fragrances, or rubbers; irritant contact dermatitis from repeated exposure to irritants like detergents, solvents, or soaps; and contact urticaria/protein contact dermatitis which is linked to IgE-mediated reactions to proteins such as latex or foodstuffs. Endogenous causes originate within the individual, most commonly atopic hand eczema, which is associated with atopic dermatitis, asthma, or hay fever. Clinical (morphological) subtypes, with no specific cause identified, include acute recurrent vesicular hand eczema (pompholyx) with vesicular eruptions, hyperkeratotic eczema with thickened

[1] Menné T, Johansen JD, Sommerlund M, Veien NK. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. Contact dermatitis. 2011 Jul;65(1):3-12.

[2] Apfelbacher, C, Bewley, A, Molin, S, et al. 2024, 'Prevalence of Chronic Hand Eczema in adults: A cross-sectional multi-national study of over 60,000 respondents in the general population. Poster presentation #3', paper presented at European Society of Contact Dermatitis Congress, Dresden, Germany.

[3] Thyssen, JP, Schuttelaar, MLA, Alfonso, JH, et al. 2022, 'Guidelines for diagnosis, prevention, and treatment of hand eczema', Contact Dermatitis, vol. 86, no. 5, pp. 357–378.

fissured palms, nummular eczema with coin-shaped lesions, and pulpitis affecting the fingertips.

4.4 Delgocitinib is a pan-Janus kinase (JAK) inhibitor that acts on all four JAK enzymes, i.e. JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2). The submission noted that more than half of patients with hand eczema present with mixed subtypes, each involving distinct T helper (CD4-positive) cell responses. Despite this variability, all forms share activation of JAK-STAT signalling pathways. By inhibiting all four JAK enzymes, delgocitinib targets the shared inflammatory mechanisms across subtypes, offering a therapeutic approach that addresses the heterogeneous nature of CHE.

4.5 For the treatment of CHE, delgocitinib is applied twice daily to clean, dry skin on the hands and wrists. Treatment continues until the skin appears clear or nearly clear. Patients should avoid using other topical products immediately before or after applying delgocitinib. In the event of a flare or recurrence of CHE symptoms, twice-daily application can be restarted on affected areas as needed. No dosing adjustment was recommended in the submission or the draft PI.

4.6 The ESC considered that as a topical therapy that would be used in an episodic manner by most patients, the proposed positioning of delgocitinib may not reflect its likely use in practice. The ESC acknowledged the populations in the trials had an inadequate response or were unable to receive TCS, and had a minimum disease severity defined by diagnostic criteria (HESD itch score). However, the ESC also considered that in practice, many patients with an inadequate or partial response to TCS would likely continue suboptimal treatment with the strongest tolerated therapy. This would lead to flow-on implications including how delgocitinib was likely to be positioned in the treatment algorithm, comparator selection, and clinical relevance of the presented clinical and economic analyses.

4.7 The Pre-PBAC Response reiterated that the place in therapy proposed in the submission reflected the clinical evidence for delgocitinib in the Australian context and noted that, in other markets, alitretinoin was available as a therapeutic alternative in CHE.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The submission nominated SoC as the main comparator in moderate to severe CHE treatment. The submission positioned delgocitinib before systemic therapy, stating that SoC was the only relevant option given the absence of PBS-listed topical therapies. SoC included non-medicated emollient use alone and avoidance of known irritants and allergens.

5.2 During the evaluation, the makeup of SoC was considered adequate only for the small proportion of patients who are contraindicated to TCS. The PBAC has previously noted that in clinical practice, for patients who have an intolerance to TCS or who have failed to achieve satisfactory control with TCS, some degree of continuing TCS use is likely

for symptom management, and TCS should be included as a comparator (paragraph 7.5, crisaborole PSD, November 2018 PBAC meeting). It was also noted that tacrolimus ointment 0.1%, which is a topical calcineurin inhibitor (TCI) was recommended in July 2025 for the treatment of moderate to severe atopic dermatitis and is potentially a relevant comparator. The Pre-Sub-Committee Response (PSCR) stated that the proposed treatment algorithm separated SoC from first-line pharmacotherapy (which consists of TCS or topical calcineurin inhibitors (TCIs)) and that for the target delgocitinib population, first line pharmacotherapy was inadequate or not an option. Therefore, the comparison to SoC was valid for assessing the clinical claims. The PSCR further noted advice from the NICE EAG Report for delgocitinib that suggested 'TCIs are often used as first line optimisation alongside TCS and not as a monotherapy approach in the target patient population', whereas delgocitinib is intended to be a sole PBS subsidised therapy for CHE for patients meeting the relevant criteria.

5.3 The ESC considered that, given the impact that moderate to severe CHE has on patients' daily activity of living, patients are unlikely to only be treated with SoC consisting of non-medicated emollients. The ESC accepted that TCS are not an appropriate comparator for patients contraindicated to or who cannot tolerate or use TCS, but that for the population who experience an inadequate response to TCS, suboptimal TCS may be an appropriate comparator, as patients may continue suboptimal treatment in practice. Furthermore, the ESC considered that tacrolimus (compounded or otherwise) may be a relevant comparator for, at least, the atopic subtype of chronic hand eczema. The ESC also noted that the 2019 Cochrane Review[4], 'Interventions for hand eczema', concluded tacrolimus 0.1% probably improves investigator-rated symptom control measured after three weeks compared to vehicle.

5.4 Dupilumab was nominated as a supplementary comparator due to its widespread use in clinical practice for the atopic subtype of CHE. Upadacitinib may have also been considered an alternative treatment as it is used in the same population as dupilumab. The ESC considered that, as a topical therapy that would be used in an episodic manner by most patients, delgocitinib is unlikely to replace systemic treatments in a substantial proportion of patients.

5.5 The submission also stated that some dermatologists may prescribe dupilumab (and upadacitinib) for CHE subtypes beyond those explicitly covered by their PBS listings (i.e. non atopic subtypes), supporting its inclusion for comparison where treatment overlap exists. Atopic dermatitis affecting the hands is part of systemic atopy, associated with immune dysregulation and barrier dysfunction, and often occurs alongside lesions elsewhere. CHE, by contrast, is generally limited to the hands and results from repeated exposure to irritants or allergens. Atopic dermatitis is usually erythematous, scaly, and lichenified, while CHE often shows vesicles, hyperkeratosis,

[4] Christoffers WA, Coenraads PJ, Svensson Å, Diepgen TL, Dickinson-Blok JL, Xia J, Williams HC. Interventions for hand eczema. Cochrane Database of Systematic Reviews 2019, Issue 4. Art. No.: CD004055. DOI: 10.1002/14651858.CD004055.pub2.

or fissures. The main distinctions are aetiology, systemic involvement, and morphology. The use of dupilumab for non-atopic CHE may result from either uncertainty in identifying the clinical features or subtype, or from off-label use based on the assumption that the underlying pathophysiology would still respond to dupilumab or upadacitinib.

5.6 Phototherapy could be considered a relevant comparator to delgocitinib as it is a publicly funded, non-systemic treatment used in moderate to severe CHE when TCS are unsuitable. It occupies a similar place in therapy to delgocitinib prior to systemic immunosuppressants, provides a non-pharmacological alternative, and was a key comparator to delgocitinib in the National Institute for Health and Care Excellence (NICE) assessment[5]. While the submission argued against its use due to access issues[6], these challenges are not unique to phototherapy and also apply to other specialist-delivered treatments. The PBAC previously noted that there may be some use of phototherapy in patients with chronic moderate to severe atopic dermatitis; however, there was likely to be limited clinical evidence to inform a comparison with dupilumab (paragraph 5.4, dupilumab, PSD, July 2019 PBAC meeting). Further, uptake of phototherapy was limited by patient access to this service and the considerable out-of-pocket expenses associated with it (paragraph 5.3, dupilumab, PSD, July 2019 PBAC meeting). The PSCR stated that the MBS listing for phototherapy (item 14050) restricted use to when topical therapy has failed or is inappropriate, and it would therefore be positioned after delgocitinib in the treatment algorithm.

5.7 The submission noted that immunosuppressants including methotrexate, azathioprine, ciclosporin, and mycophenolate mofetil, were either associated with greater safety concerns or lacked formal listing making them unsuitable comparators. Methotrexate, azathioprine, ciclosporin, and mycophenolate mofetil have not been considered as comparators for other treatments, including dupilumab and upadacitinib. The PBAC previously considered ciclosporin A to be an additional relevant comparator to dupilumab (paragraph 5,4, dupilumab, PSD, July 2019 PBAC Meeting). However, it acknowledged that ciclosporin was associated with considerable toxicity, of note renal toxicity and the need to limit the duration of exposure (paragraph 6.35, dupilumab, PSD, July 2019 PBAC Meeting).

For more detail on PBAC's view, see section 7 PBAC outcome.

[5] https://www.nice.org.uk/guidance/GID-TA11506/documents/consultation-document

[6] In its assessment of dupilumab for patients aged 12 years and older with severe atopic dermatitis inadequately controlled by topical therapies, the PBAC noted that the use of phototherapy in Australia was limited due to its restricted availability and the significant burden it places on patients in terms of treatment frequency, duration, and cost (paragraph 7.19, dupilumab, PSD, March 2020 PBAC Meeting).

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician discussed the treatment landscape in Australia, the burden of disease on patients and the clinical need for new and effective therapies. The clinician also discussed the results of the clinical trials, that demonstrated patients have improvement and restoration of dexterity and that many patients continued to have clear skin for extended periods following treatment with delgocitinib. The clinician highlighted that patients who receive topical corticosteroids suffer adverse events and thinning of the skin with continuous use and noted the listing of delgocitinib would be particularly advantageous for regional and rural patients where access to dermatologists was limited and managing systemic therapies can be complicated.

Consumer inputs

6.2 The PBAC noted and welcomed the input from individuals (2), health professionals (2), medical organisation the Australasian College of Dermatologists (ACD), and consumer organisations Eczema Support Australia and Eczema Association Australia, all supporting the listing of delgocitinib.

6.3 The Committee noted the input from individuals described CHE as a relentless condition that causes both physical pain and emotional distress, with daily tasks such as typing, using door handles and opening packaging described as painful obstacles, with a frequent need to take time off work. The input also highlighted the benefits if general practitioners were able to prescribe delgocitinib, due to issues accessing and affording a dermatologist.

6.4 The PBAC noted the input from health professionals described delgocitinib as a novel, safe and effective treatment that may prevent the need for systemic therapies and discussed the unwanted side effects the arise from long-term use of topical corticosteroids. The input also outlined the limitations of other treatments such as phototherapy, systemic immunosuppressants and targeted therapies including issues accessing specialists to prescribe and/or administer therapies, long-term effectiveness and known safety issues with some therapies.

6.5 The PBAC noted the input from the ACD highlighted the negative impact of CHE on patients and supported the listing of delgocitinib, stating it would be of significant benefit in improving affordability, equitable access and quality of life for patients.

6.6 The PBAC welcomed the input from Eczema Support Australia, which presented patient voices and the results of a September 2025 hand eczema survey, where patients reported barriers to care included cost of treatment, long wait times and the impacts of their condition on work and personal life. The PBAC also noted the input noted TCS, where used appropriately, remain the cornerstone of eczema treatment, but highlighted targeted therapies such as dupilumab are only available for the atopic

dermatitis subtype of CHE and there is a clear gap for patients who need a practical, effective non-steroidal option when TCS are no longer sufficient or appropriate.

6.7 The PBAC also welcomed the input from Eczema Association Australia, which discussed the current treatment landscape for CHE in Australia, and highlighted many patients report only partial or short-term relief with currently available treatments such as TCS, with clear risks from long-term use, and that systemic immunosuppressants have a poor safety profile, and phototherapy is difficult and costly to access. The PBAC also noted the input discussed CHE the burden of disease and highlighted the need for new safe and effective therapies that are affordable and accessible. The input also discussed the potential for delgocitinib to have a positive and transformative effect on quality of life for some patients.

Clinical trials

6.8 The submission was primarily based on 2 head-to-head randomised controlled trials comparing delgocitinib to a cream vehicle (representing SoC):

- DELTA 1 trial (N=487) enrolled adults with moderate to severe CHE and compared delgocitinib (n=325) to vehicle (n=162) in patients with hand eczema symptom diary (HESD) itch score (weekly average) of ≥4 points [full analysis set (FAS) and safety analysis set (SAF): 487]
- DELTA 2 trial (N=473) enrolled adults with moderate to severe CHE and compared delgocitinib (n=314) to vehicle (n=159) in patients with HESD itch score (weekly average) of ≥4 points [FAS and SAF: 472].

6.9 The submission identified an extension study from the pivotal trials:

- DELTA 3 study (N=810) enrolled patients who completed either DELTA 1 or DELTA 2. DELTA 3 (N=801) was an open-label study in which patients could apply delgocitinib cream as needed based on investigator's global assessment for CHE (IGA-CHE) score.

6.10 The submission did not identify any head-to-head trials comparing delgocitinib and dupilumab. As a result, a matching-adjusted indirect comparison (MAIC) was conducted using pooled data from the DELTA 1 and DELTA 2 trials and published data from the LIBERTY-AD-HAFT dupilumab trial, with placebo as the common comparator:

- LIBERTY-AD-HAFT trial enrolled adult and adolescent patients with moderate to severe atopic hand and foot dermatitis and compared dupilumab (n= 67) and placebo (n=66).

6.11 Details of the trials presented in the submission are provided in Table 2.

Table 2: Key trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Delgocitinib trials		
DELTA 1	Clinical Trial Report LP0133-1401: A phase 3 clinical trial to confirm efficacy and evaluate safety of twice-daily delgocitinib cream 20 mg/g compared with cream vehicle for a 16-week treatment period in adult subjects with moderate to severe chronic hand eczema (DELTA 1)	*CSR*, March 2023.
DELTA 2	Clinical Trial Report LP0133-1402: A phase 3 clinical trial to confirm efficacy and evaluate safety of twice-daily delgocitinib cream 20 mg/g compared with cream vehicle for a 16-week treatment period in adult subjects with moderate to severe chronic hand eczema (DELTA 2). Clinical trial report, v1.0. Trial ID:	*CSR*, April 2023.
	Thaci D, Gooderham M, Lovato P, et al. Systemic exposure and bioavailability of delgocitinib cream in adults with moderate to severe Chronic Hand Eczema.	Journal of European Academy Dermatology and Venerology 2025; 00: 1-10.
DELTA 1 and DELTA 2 trials	Bissonnette R, Warren RB, Pinter A, et al. Efficacy and safety of delgocitinib cream in adults with moderate to severe chronic hand eczema (DELTA 1 and DELTA 2): results from multicentre, randomised, controlled, double-blind, phase 3 trials.	Lancet 2024; 404(10451): 461–473.
Non-randomised or open label-studies		
DELTA 3	Clinical Trial Report LP0133-1403: A phase 3 extension trial of DELTA 1 and DELTA 2 to evaluate the long-term safety of a twice-daily treatment with delgocitinib cream 20 mg/g as needed for up to 36 weeks in adult subjects with chronic hand eczema (DELTA 3).	*CSR*, January 2024.
	Gooderham M, Molin S, Bissonnette R, Worm M, Crépy MN, Stingeni L, Warren RB, Schliemann S, Schuttelaar ML, Ferrucci S, Serra-Baldrich E, Silverberg JI, Balita-Crisostomo CL, Oesterdal ML, Plohberger U, Agner T. Long-term safety and efficacy of delgocitinib cream for up to 52 weeks in adults with Chronic Hand Eczema: results of the phase 3 open-label extension DELTA 3 trial following the DELTA 1 and 2 trials.	Journal of the American Academy of Dermatology 2025; S0190-9622(25): 00424-4.
Dupilumab vs placebo		
LIBERTY-AD-HAFT	Simpson, EL; Silverberg, JI; Worm, M; Honari, G; Masuda, K; Sygula, E; Schuttelaar, MLA; Mortensen, E; Laws, E; Akinlade, B; Patel, N; Maloney, J; Paleczny, H; Delevry, D; Xiao, J; Dubost-Brama, A; Bansal, A. Dupilumab treatment improves signs, symptoms, quality of life and work productivity in patients with atopic hand and foot dermatitis: results from a phase 3, randomized, double-blind, placebo-controlled trial.	Journal of the American Academy of Dermatology 2024; 90(6): 1190-1199.
	Margitta Worm, Eric L Simpson, Golara Honari, et al. 566 - Efficacy of dupilumab treatment in atopic hand and foot dermatitis across morphological subtypes: results from a phase 3, randomized, double-blind, placebo-controlled trial.	British journal of dermatology 2024;190(S2): ii60.
	A Study to Evaluate the Efficacy and Safety of Dupilumab in Adult and Adolescent Patients With Moderate-to-Severe Atopic Hand and Foot Dermatitis (Liberty-AD-HAFT)	Date not provided.

Source: Table 20, pp63-66 of the submission.
CSR = clinical study report.
Note: Poster or conference presentations or abstract-only publications presented by the submission are excluded from the Table above.

6.12 A claim of superior efficacy for delgocitinib compared to SoC (represented by cream vehicle) was made on the main outcome: IGA-CHE Treatment Success (TS) from the DELTA 1 and 2 trials defined as an IGA-CHE score of 0 [clear] or 1 [almost clear] with at least a 2-step improvement at Week 16, and key secondary outcomes: hand eczema

severity index (HECSI), hand eczema symptom diary (HESD), and hand eczema impact scale (HEIS) scores and dermatology life quality index (DLQI).

6.13 A claim of non-inferior efficacy for delgocitinib compared to dupilumab was made on the primary outcome of IGA-CHE (from DELTA 1 and DELTA 2 trials) or hand foot - investigator global assessment (HF-IGA) (from LIBERTY-AD-HAFT trial) score 0/1 at Week 16 and secondary outcomes of HECSI-75, HECSI-90 and HECSI score change from baseline at Week 16.

6.14 The DLQI has been included in previous PBAC submissions. The IGA-CHE, HECSI, HESD or HEIS have not been included in previous PBAC submissions.

6.15 Table 3 presents definitions of key outcomes and nominated minimal clinically important difference (MCID) values.

Table 3: Key outcomes and their definitions

Outcome	Definition	Proposed MCID and response
IGA-CHE	A 5-point scale used by clinicians to evaluate the overall severity of a patient's CHE. The assessment incorporates multiple clinical signs, including erythema, scaling, hyperkeratosis, vesiculation, oedema, and fissures, to determine a single global score for the patient's disease (0 is clear and 4 is severe).	MCID: An IGA-CHE score of 0 (clear) or 1 (almost clear) with a ≥ 2-step improvement from baseline. Response: **Health state** / **IGA - CHE** Full response: 0 (Clear) or 1 (Almost clear) Partial response: 2 (Mild) Low response: 3 with 1-point improvement from baseline (Moderate) Insufficient response: 3 without improvement from baseline or IGA-CHE 4 (Severe)
HECSI	An investigator-rated assessment tool that measures hand eczema severity by scoring 6 symptoms, including erythema, infiltration, vesicles, fissuring, scaling, and oedema, across 5 specific hand areas (fingertips, fingers, palms, back of hands, and wrists). The total score, ranging from 0 to 360, is calculated by multiplying the sum of the intensity scores for the 6 signs by the % of affected skin area in each of the 5 regions.	MCID (2 proposed): an 8.3-point improvement to capture smaller but clinically meaningful changes, and a 41-point threshold to reflect larger, more conservative improvements. Response: **Health state** / **HECSI** Full response: ≥90 Partial response: 75 to 89 Low response: 50 to 74 Insufficient response: < 50
HESD	A patient-reported outcome tool that tracks the severity of 13 symptoms over 24 hours on a 0-10 scale. Patients are asked to report their worst symptoms, such as itching, pain, or cracked skin, to provide data on symptom fluctuations over time.	MCID: An improvement of ≥ 4 points in the 7-day (weekly) average for the HESD itch score, HESD pain score and the HESD scores
HEIS	A self-administered patient-reported questionnaire used to assess the impact of hand eczema on a person's daily life, covering symptoms like itching, pain, and frustration, and the resulting difficulty with activities like housework and work, over a 1-week recall period. It consists of 9 items that assess domains related to the ability to use cleaning products, quality of sleep, embarrassment, and difficulty with daily tasks and work, but it does not directly measure clinical signs of eczema.	MCID: 1.3 points of ≥ 1.3 points in HEIS score and HEIS PDAL score.
DLQI	A 10-item questionnaire that measures how skin diseases, including eczema, affect a patient's quality of life. It uses a 4-point scale (0–3), is reported by the patient, and assesses areas like symptoms, daily activities, and relationships over the past week. The total score ranges from 0 (no impact) to 30 (maximum impact), with higher scores indicating greater impairment.	MCID: Improvement of ≥4 points

Source: Compiled during the evaluation based on pp112-113, 118, 122-126 of the submission; Attachment 7 of the submission.
CHE = Chronic hand eczema; DLQI = Dermatology life quality index; IGA-CHE = Investigator's global assessment for chronic hand eczema; HECSI = Hand eczema severity index; HESD = Hand eczema severity diary; HEIS = Hand eczema itch scale; MCID = Minimal clinically important difference; PDAL = Proximal daily activity limitations.

6.16 The key features of the delgocitinib trials and study are summarised in Table 4.

Table 4: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
Delgocitinib 20 mg/g cream BD or cream vehicle						
DELTA 1	487	R, DB, MC 16 weeks	Low	Adult participants with moderate to severe chronic hand eczema for whom TCS is ineffective or inappropriate.	Primary: IGA-CHE TS at Week 16 (% responders) Secondary: • HECSI-75 at Weeks 8 and 16. • HECSI-90 at Week 16. • IGA-CHE TS at Weeks 4 and 8. • % change in HECSI score from baseline to Week 16. Exploratory: HRQoL: EQ-5D-5L + VAS (Weeks: 1, 4, 8, 12, and 16)	Transition probabilities (response/ treatment effects for different severity levels %, non-response, relapse until Week 12); Utilities
DELTA 2	473				Similar to DELTA 1 + pharmacokinetic assessments (Weeks 1, 4 and 16)	
Delgocitinib 20 mg/g as needed (OLE)						
DELTA 3	801	OLE Efficacy: 36 weeks Safety: 36-38 weeks (Total: 16+ 36 = 52 weeks)	High	Participants from DELTA 1 & 2	Primary: number of TEAEs observed from baseline to Week 38. Secondary: IGA-CHEs, HECSI, HECSI-75, 90 outcomes from baseline to Week 36 Several exploratory outcomes including EQ-5D-5L	Transition probabilities (response or non-response, relapse beyond Week 12, discontinuation)
Dupilumab vs placebo						
LIBERTY-AD-HAFT[a]	133	R, DB, MC 16 weeks + 12 weeks follow-up	Low	Adults (≥18 years) and adolescents (≥12 to <18 years) with moderate-to-severe H/F AD	Primary: HF-IGA Key secondary: proportion of patients with ≥4-point reduction in HF-Peak Pruritus NRS at Week 16; HECSI-75; Change in HECSI score from baseline to Week 16.	Used as the basis for a cost-minimisation approach, informed by the non-inferiority claim between delgocitinib and dupilumab.

Source: Table 98, p167 of the submission; pp111-121 of the submission

AE = Adverse Event; AUC = Area Under the Curve; BD = twice daily; DB = Double blind; DLQI = Dermatology Life Quality Index; EQ-5D-5L = EuroQol 5 Dimensions 5 Levels; HECSI = Hand Eczema Severity Index; HECSI-75 = Hand Eczema Severity Index 75% improvement; HECSI-90 = Hand Eczema Severity Index 90% improvement; HEIS = Hand Eczema Impact Scale; HEIS PDAL = Hand Eczema Impact Scale – Proximal Daily Activity Limitation; HESD = Hand Eczema Symptom Diary; HRQoL = Health-Related Quality of Life; IGA-CHE TS = Investigator's Global Assessment for Chronic Hand Eczema Treatment Success; MC = Multi-centre; OLE = Open label extension; PRO = Patient-Reported Outcome; R = Randomised; TEAE = Treatment-Emergent Adverse Event; TCS = Topical Corticosteroid; VAS = Visual Analogue Scale; WPAI: CHE = Work Productivity and Activity Impairment Questionnaire for Chronic Hand Eczema.

6.17 The overall risk of bias was assessed to be low for the pivotal DELTA 1 and DELTA 2 trials, as blinding was maintained throughout the trials. However, the appropriateness of imputing all missing data in the DELTA 1 and DELTA 2 trials as non-response for binary outcomes, and applying worst observation carried forward (WOCF, including baseline values) for continuous outcomes, was uncertain. While these methods avoided overestimation of treatment effect, they may also introduce bias through

systematic underestimation, and thus, the overall implication of the approach was not fully clear.

6.18 The submission did not present the risk of bias assessment of the LIBERTY-AD-HAFT trial used in the indirect comparison of delgocitinib vs dupilumab. However, the overall risk of bias in the LIBERTY-AD-HAFT trial was assessed as low given its randomised, double-blind study design.

6.19 There were differences between the pivotal DELTA 1 and DELTA 2 trials, including:

- DELTA 1 enrolled more severe patients compared to DELTA 2, which may reduce treatment responsiveness or alter safety outcomes. This was reflected in the primary efficacy outcome, with the treatment effect in the DELTA 1 trial being notably lower than that observed in the DELTA 2 trial.
- DELTA 1 had higher rates of atopic hand eczema (44.6% vs 27.1%) and allergic contact dermatitis (17.2% vs 10.4%). In contrast, DELTA 2 had greater proportions of irritant contact dermatitis (23.9% vs 15.4%), contact urticaria (0.2% vs 0%), vesicular hand eczema (11.2% compared to 7.0%), and hyperkeratotic hand eczema (27.3% vs 15.8%). These differences in subtype distribution may affect treatment response. The submission did not present trial-specific subgroup analyses by CHE subtype; efficacy by subtype was only reported for the pooled DELTA 1 and 2 trials.

6.20 There were differences between the DELTA 1/2 and LIBERTY-AD-HAFT trials, including, age (adults vs 12+), anatomical sites (CHE vs atopic dermatitis in hands or feet), and disease duration (CHE for ≥3 months or ≥2 relapses per year vs atopic dermatitis in adults for ≥ 3 years and adolescents for ≥ 1 year) which may have affected the assumption of transitivity.

Comparative effectiveness

Comparison with SoC

6.21 Table 5 presents the results for the primary and key secondary outcomes from the DELTA 1 and DELTA 2 trials at 16 weeks. The ESC noted DELTA 3 provided some data out to Week 52 that was supportive of the effectiveness and safety of delgocitinib over the longer term.

Table 5: Results of primary, key secondary and exploratory outcomes across the DELTA 1 and DELTA 2 trials

Outcome at Week 16	Trial ID	Delgocitinib, n/N (%)	Vehicle, n/N (%)	Risk Difference, (95% CI)
Primary outcome (responder)				
IGA-CHE TS[a]	DELTA 1	64/325 (19.7)	16/162 (9.9)	**9.8% (3.6, 16.1)**
	DELTA 2	91/313 (29.1)	11/159 (6.9)	**22.2% (15.8, 28.5)**
	Pooled DELTA 1 and 2	155/638 (24.3)	27/321 (8.4)	**15.9% (11.4, 20.4)**
Key Secondary outcomes (categorical)				
HECSI-75	DELTA 1	160/325 (49.2)	38/162 (23.5)	**25.7% (17.2, 34.3)**
	DELTA 2	155/313 (49.5)	29/159 (18.2)	**31.3% (23.1, 39.5)**
HECSI-90	DELTA 1	96/325 (29.5)	20/162 (12.3)	**17.2% (10.1, 24.3)**
	DELTA 2	97/313 (31.0)	14/159 (8.8)	**22.2% (15.4, 29.0)**

Outcome at Week 16	Trial ID	Delgocitinib, n/N (%)	Vehicle, n/N (%)	Risk Difference, (95% CI)
HESD itch reduction ≥4 points[b]	DELTA 1	152/325 (47.1)	37/161 (23.0)	**24.1% (15.5, 32.6)**
	DELTA 2	146/309 (47.2)	31/156 (19.9)	**27.4% (19.0, 35.8)**
HESD reduction ≥4 points[b]	DELTA 1	146/309 (47.2)	38/156 (24.4)	**22.8% (14.0, 31.7)**
	DELTA 2	137/308 (44.5)	32/153 (20.9)	**23.7% (15.1, 32.2)**
HESD pain reduction ≥4 points[b]	DELTA 1	143/291 (49.1)	41/149 (27.5)	**21.7% (12.4, 30.9)**
	DELTA 2	143/294 (48.6)	32/141 (22.7)	**26.0% (17.0, 35.1)**
DLQI reduction ≥4 points[b]	DELTA 1	227/291 (74.4)	74/149 (50.0)	**24.5% (15.0, 33.9)**
	DELTA 2	216/294 (72.2)	70/141 (45.8)	**26.4% (17.0, 35.9)**
Key Secondary outcomes (continuous)				
Outcome	**Trial ID**	**Delgocitinib, LS Mean (SE)**	**Vehicle, Mean (SE)**	**Mean Difference, (95% CI)**
HECSI scores, change from baseline	DELTA 1	50.9[c]	32.0[c]	**18.6 (11.3, 25.9)[d]**
	DELTA 2	44.3[c]	25.0[c]	**22.7 (17.1, 28.2)[d]**
HECSI % change from baseline	DELTA 1	-56.5 (3.4)	-21.2 (4.8)	**-35.2 (-46.7, -23.8)**
	DELTA 2	-58.9 (3.2)	-13.4 (4.5)	**-45.5 (-56.4, -34.6)**
HESD itch change from baseline	DELTA 1	-3.6 (0.2)	-1.9 (0.2)	**-1.7 (-2.3, -1.2)**
	DELTA 2	-3.4 (0.2)	-1.4 (0.2)	**-2.0 (-2.5, -1.4)**
HESD total score change from baseline	DELTA 1	-3.4 (0.1)	-1.7 (0.2)	**-1.7 (-2.2, -1.2)**
	DELTA 2	-3.2 (0.1)	-1.4 (0.2)	**-1.9 (-2.4, -1.4)**
HESD pain change from baseline	DELTA 1	-3.4 (0.2)	-1.8 (0.2)	**-1.6 (-2.1, -1.0)**
	DELTA 2	-3.3 (0.2)	-1.3 (0.2)	**-2.0 (-2.6, -1.5)**
DLQI change from baseline	DELTA 1	-7.6 (0.3)	-3.9 (0.4)	**-3.6 (-4.7, -2.6)**
	DELTA 2	-7.0 (0.3)	-3.1 (0.5)	**-3.9 (-5.0, -2.8)**
HEIS change from baseline	DELTA 1	-1.46 (0.05)	-0.82 (0.08)	**-0.64 (-0.83, -0.45)**
	DELTA 2	-1.45 (0.06)	-0.64 (0.08)	**-0.81 (-0.99, -0.62)**
HEIS PDAL change from baseline	DELTA 1	-1.46 (0.06)	-0.86 (0.08)	**-0.60 (-0.79, -0.40)**
	DELTA 2	-1.48 (0.06)	-0.66 (0.08)	**-0.82 (-1.01, -0.62)**
Key exploratory outcome (continuous)				
Mean (SE) change in EQ-5D-5L index score from baseline	DELTA 1	0.176 (0.011)[e]	0.073 (0.015)	**0.10 (0.07, 0.14)**
	DELTA 2	0.157 (0.011)	0.049 (0.015)	**0.11 (0.07, 0.15)**

Source: Based on Table 83, p140; Table 84, p142; Table 85, p143; Table 89, p148 of the submission; p300 of the DELTA 1 CSR; p304 of the DELTA 2 CSR.

CI = confidence interval; DLQI = Dermatology Life Quality Index; EQ-5D-5L = EuroQol-5 Dimensions-5 Levels; FAS=full analysis set; HECSI = Hand Eczema Severity Index; HECSI-75 = at least 75% improvement in HECSI score from baseline; HECSI-90 = at least 90% improvement in HECSI score from baseline; HEIS = Hand Eczema Impact Scale; 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; LSMean = least squares mean; N = number of patients with data available at baseline; PDAL = Proximal Daily Activity Limitations; SE = standard error, Wk = week.

Bold indicates statistically significant results.

[a] Results from the primary analysis only are presented, as the sensitivity analyses in the submission did not differ substantially from the primary analysis.

[b] An improvement of ≥ 4 points in 7-day (weekly) average for the HESD Itch score, HESD Pain score and the HESD scores represented an MCID. An improvement of ≥ 4 points from baseline for the DLQI score also represented an MCID.

[c] % difference from baseline to Week 16 in DELTA 1 in delgocitinib vs vehicle arms: 65.6% vs 41.4%; DELTA 2: 68.9% vs 36.9%.

[d] Mean(SD) from Week 16 values used to estimate the mean differences and 95% CIs. Calculations were done during the evaluation using MedCalc. P-values for mean differences in both DELTA 1 and DELTA 2 trials were <0.0001.

[e] Corrected during the evaluation.

6.22 At Week 16, the proportion of patients achieving IGA-CHE TS was significantly higher in the delgocitinib arm compared with the vehicle arm in both trials, with a risk difference of 9.8% (95% CI: 3.6, 16.1; p=0.0055) in DELTA 1 and 22.2% (95% CI: 15.8, 28.5; p<0.0001) in DELTA 2.

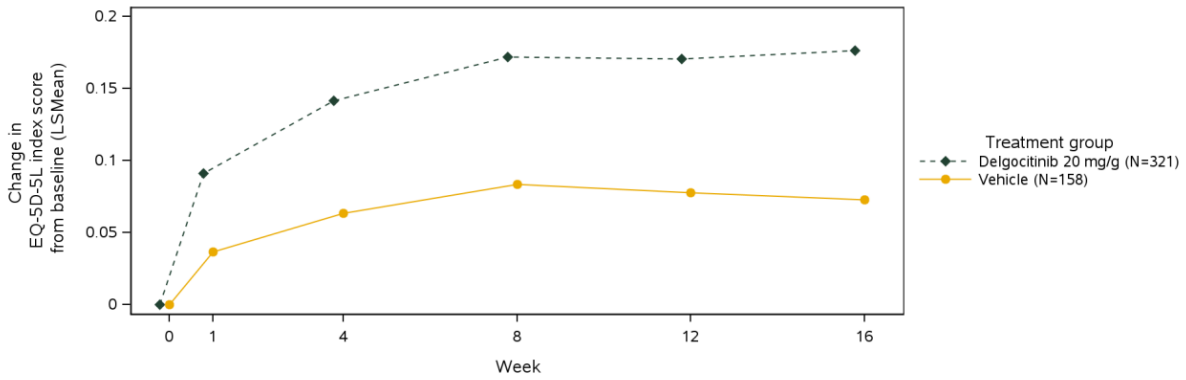
6.23 During the 16-week treatment period in DELTA 1 and DELTA 2, the treatment effect of delgocitinib vs vehicle increased from Week 1 to Week 8. There were significant differences at Week 4 and the difference remained stable after Week 8.

6.24 Key secondary outcomes in the DELTA 1 and DELTA 2 trials consistently favoured delgocitinib over vehicle, with significant benefits observed across HESD, DLQI, HECSI, and EuroQoL 5 dimensions 5 levels (EQ-5D-5L) measures.

6.25 Quality of life, assessed by DLQI, showed significantly higher proportions of patients achieving a ≥4-point reduction at Week 16 with delgocitinib (differences of 24.5% and 26.4%, both p<0.001), and greater mean score improvements (differences of −3.6 and −3.9; both p<0.001).

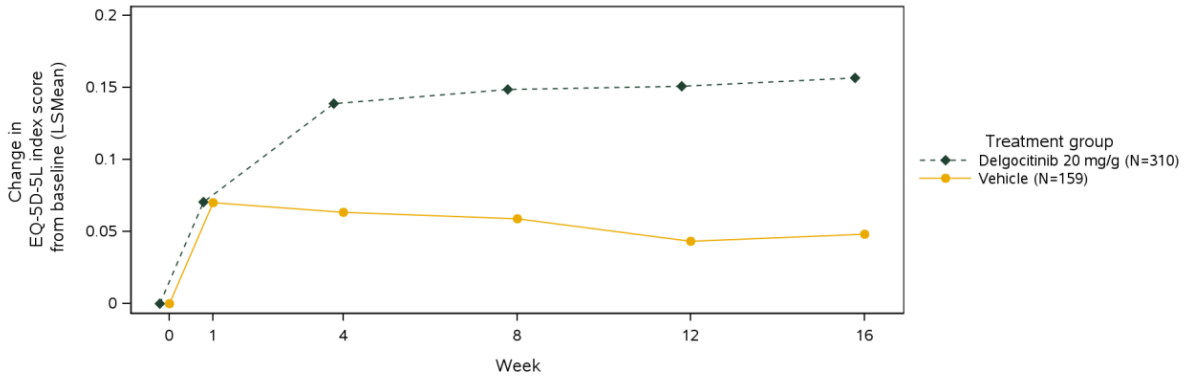
6.26 At Week 16, the EQ-5D-5L Index score improved in both trials (see Table 5 and Figure 1 and Figure 2). In DELTA 1, the delgocitinib arm improved by 0.176 (SE = 0.011) vs 0.073 (SE = 0.015) in the vehicle arm. In DELTA 2, the delgocitinib arm improved by 0.157 (SE = 0.011) vs 0.049 (SE = 0.015) in the vehicle arm. The treatment differences were 0.103 (95% CI: 0.067, 0.140) and 0.108 (95% CI: 0.071, 0.145), respectively, and both were statistically significant.

Figure 1: Change in EQ-5D-5L index score in DELTA 1 from baseline to Week 16



Source: Panel 53, p95 of the DELTA 1 CSR
EQ-5D-5L = EuroQol 5-Dimension Health Questionnaire 5 Level; LS = least squares

Figure 2: Change in EQ-5D-5L index score in DELTA 2 from baseline to Week 16



Source: Panel 53, p95 of the DELTA 2 CSR
EQ-5D-5L = EuroQol 5-Dimension Health Questionnaire 5 Level; LS = least squares

6.27 The submission presented efficacy results by CHE subtype for pooled data from the DELTA 1 and DELTA 2 trials at 16 weeks. Overall, the subgroup findings demonstrated that delgocitinib achieved more favourable outcomes than the vehicle across nearly all CHE subtypes at Week 16. The ESC noted the results in hyperkeratotic eczema were somewhat less supportive than for the other subtypes.

6.28 Results from the DELTA 3 study at Week 52 suggested considerable variability in treatment effects across CHE subtypes. Subtype-specific response rates indicated higher efficacy in irritant contact dermatitis, with IGA-CHE TS achieved by 75.7% of patients and HECSI-75 by 92.5%. Similar high responses were seen in vesicular hand eczema (IGA-CHE TS: 72.5%; HECSI-75: 87.7%) and allergic contact dermatitis (IGA-CHE TS: 66.0%; HECSI-75: 89.4%). Atopic hand eczema showed more modest responses (IGA-CHE TS: 58.9%; HECSI-75: 84.7%), while hyperkeratotic eczema demonstrated the lowest rates (IGA-CHE TS: 38.2%; HECSI-75: 68.6%).

Comparison with dupilumab

6.29 The submission presented a MAIC between delgocitinib and dupilumab based on the DELTA 1 and DELTA 2 and LIBERTY-AD-HAFT trials. Although the LIBERTY-AD-HAFT trial included patients with atopic dermatitis of the hands or feet, patients with atopic dermatitis of the feet (n = 4) were not excluded. The submission restricted the analysis of the DELTA 1 and DELTA 2 trials to the CHE atopic subtype population as the LIBERTY-AD-HAFT trial enrolled patients with atopic dermatitis only. The following effect modifiers were considered: sex, race, baseline disease severity (HECSI score), age and CHE subtype (restricted to atopic CHE).

6.30 A propensity score weighting technique was used to align the baseline characteristics of patients in the DELTA 1 and DELTA 2 trials with those in the LIBERTY-AD-HAFT trial.

6.31 Table 6 presents MAIC results for the primary outcome (HF-IGA/IGA-CHE) and secondary outcomes (HECSI-75, HECSI-90, and HECSI percentage change from baseline) for delgocitinib vs dupilumab at Week 16.

Table 6: Summary of ITC results for efficacy endpoints for delgocitinib vs dupilumab at Week 16

Endpoints	Odds Ratio (OR) – binary endpoints			Response Difference (RD) – continuous endpoints		
	Point estimate (Delgocitinib vs Dupilumab)[a]	95% CI	p-value	Point estimate (Delgocitinib vs Dupilumab)	95% CI	p-value
IGA-CHE/HF-IGA	1.1	(0.3, 3.4)	0.890	NA		
HECSI-90	1.3	(0.4, 4.9)	0.661	NA		
HECSI-75	1.2	(0.4, 3.2)	0.773	NA		
HECSI percent CfB	NA			11.7%	(-9.2%, 32.7%)	0.273

Source: Table 124, p239 of the submission.
CHE = chronic hand eczema; CfB = change from baseline; HECSI = Hand Eczema Severity Index; HF = hand and foot; IGA-CHE = Investigator Global Assessment; ITC = indirect treatment comparison; NA = not applicable.
Note: The MAIC adjusted for age, sex, race, baseline disease severity based on HECSI score and CHE subtype to minimise bias in treatment effect estimates. Analysis was restricted to atopic CHE subtype only to reflect the primary subtype in DELTA 1/2.
[a] >1 odds ratio favours delgocitinib.

6.32 The MAIC results indicated no statistically significant differences in efficacy between delgocitinib and dupilumab. However, no non-inferiority margins were specified for any of the outcomes included in the MAIC, and formal non-inferiority analyses were not undertaken.

6.33 The PSCR presented the results of an indirect treatment comparison of delgocitinib and dupilumab (based on DELTA 1 and DELTA 2 and LIBERTY-AD-HAFT) trials using the Bucher method, which also found no statistically significant differences between delgocitinib and dupilumab for HECSI-75, HECSI-90 and proportion of patients achieving an IGA score of 0/1. The ESC considered that whilst the sample sizes were larger, the analyses did not provide additional confidence to inform a claim of non-inferiority between delgocitinib and dupilumab, as the populations were more heterogeneous with this approach.

Comparative harms

6.34 Table 7 presents the results of the safety comparison for delgocitinib and vehicle based on the pivotal DELTA 1 and DELTA 2 trials.

Table 7: Summary of adverse events in DELTA 1 and DELTA 2 (SAF) during the trial period of 16 Weeks

Trial ID	Delgocitinib n/N (%)	Vehicle n/N (%)	Risk Difference (95% CI)[a]
DELTA 1			
All adverse events	147/325 (45%)	82/162 (51%)	–5.4 (–14.7, 4.0)
Serious events	6/325 (2%)	3/162 (2%)	0.0 (–3.6, 2.4)
Deaths	0/325 (0%)	0/162 (0%)	0.0 (–2.3, 1.2)
Mild	106/325 (33%)	57/162 (35%)	–2.6 (–11.6, 6.1)
Moderate	68/325 (21%)	38/162 (23%)	–2.5 (–10.7, 5.0)
Severe	12/325 (4%)	5/162 (3%)	0.6 (–3.6, 3.8)
Related to trial treatment	12/325 (4%)	13/162 (8%)	–4.3 (–9.8, –0.1)
Led to discontinuation	2/325 (1%)	6/162 (4%)	–3.1 (–7.3, –0.5)
DELTA 2			
All adverse events	143/313 (46%)	71/159 (45%)	1.0 (–8.4, 10.4)
Serious events	5/313 (2%)	3/159 (2%)	–0.3 (–3.9, 2.1)
Deaths	0/313 (0%)	0/159 (0%)	0.0 (–2.4, 1.2)
Mild	116/313 (37%)	63/159 (40%)	–2.6 (–11.9, 6.5)
Moderate	50/313 (16%)	22/159 (14%)	2.1 (–5.1, 8.5)
Severe	3/313 (1%)	4/159 (3%)	–1.6 (–5.4, 0.8)
Related to trial treatment	22/313 (7%)	11/159 (7%)	0.1 (–5.5, 4.6)
Led to discontinuation	1/313 (<1%)	5/159 (3%)	–2.8 (–6.8, –0.5)

Based on Table 102, p188 of the submission.
NA=not applicable; SAF=safety analysis set
[a] No differences were statistically significant.
Note: Adverse events of special interest, including eczema herpeticum, deep vein thrombosis, and pulmonary embolism, were not observed in any of the patients in DELTA 1 and DELTA 2 trials.

6.35 AEs were reported by a similar proportion of patients across both trials. In DELTA 1, 45% of those using delgocitinib and 51% using the vehicle experienced AEs; in DELTA 2, the rates were 46% and 45%, respectively. Most events were mild to moderate and not considered related to the treatment. No safety concerns emerged based on the assessment of AEs, laboratory results, vital signs, physical examinations, or electrocardiogram (ECG) findings.

6.36 The most commonly reported AEs included COVID-19 (10.8% vs 8.6% for delgocitinib vs vehicle in DELTA 1, 11.5% vs 12.6% in DELTA 2), nasopharyngitis (7.1% vs 8.6% for in DELTA 1, 6.7% vs 6.3% in DELTA 2), and headache (2.8% vs 2.5% in DELTA 1, 6.1% vs 5.7% in DELTA 2). Discontinuation due to AEs occurred less frequently among patients using delgocitinib (1% in DELTA 1 and <1% in DELTA 2) compared to those using the vehicle (4% in DELTA 1 and 3% in DELTA 2).

6.37 Results from DELTA 3 demonstrated that delgocitinib had a safety profile comparable to the vehicle over 36 weeks, with no emerging safety concerns and a low incidence of treatment-related AEs or serious AEs (SAEs). However, long-term safety beyond 36 weeks was uncertain. The TGA PI states that there are limited data for the use of delgocitinib in pregnant women, and it is preferable to avoid the use of delgocitinib during pregnancy. Further, the TGA PI states that non-melanoma skin cancer, primarily basal cell carcinoma, had been reported in patients treated with topical JAK inhibitors. As a precaution, periodic skin examinations of the application site are recommended for all patients, particularly those with known risk factors for skin cancer.

Benefits/harms

6.38 A summary of the comparative benefits and harms for delgocitinib vs vehicle is presented in Table 8.

Table 8: Summary of comparative benefits and harms for delgocitinib and SoC (vehicle)

	Delgocitinib n/N (%)	Vehicle n/N (%)	Event rate/100 patients		RD (95% CI)
			Delgocitinib	Vehicle	
BENEFITS					
IGA-CHE TS					
DELTA 1	64/325	16/162	20	10	**9.8 (3.6, 16.1)**
DELTA 2	91/313	11/159	29	7	**22.2 (15.8, 28.5)**
HARMS					
AEs					
DELTA 1	147/325	82/162	45	51	-5.4 (-14.8,4.0)
DELTA 2	143/313	71/159	46	45	1.1 (-8.5,10.5)
Related SAEs					
DELTA 1	6/325	3/162	2	2	-0.006 (-2.5,2.5)
DELTA 2	5/313	3/159	2	2	-0.3 (-2.8, 2,2)
AEs leading to discontinuation					
DELTA 1	2/325	6/162	1	4	-3.1 (-6.1, -0.06)
DELTA 2	1/313	5/159	0.3	3	-2.8 (-5.6, -0.04)

Source: Table 109, 186 of the submission; Table 103, p180 of the submission.
AE = adverse event; CI = confidence interval; IGA-CHE TS = Investigator's global assessment - chronic hand eczema treatment success; N = number of patients; NA = Not applicable; RD = risk difference; SAE = serious adverse event.
Note: **Bold** indicates statistically significant results.
Maximum duration of follow-up: 16 Weeks in both trials.
Italics calculated during the evaluation

6.39 On the basis of direct comparison evidence from the DELTA 1 and DELTA 2 trials, for every 100 patients treated with delgocitinib in comparison with vehicle (SoC) over a maximum duration of exposure of 16 weeks:

- Approximately 10 to 22 more patients would achieve an IGA-CHE TS, i.e. an IGA-CHE score of 0 [clear] or 1 [almost clear] with a ≥2-step improvement from baseline.
- There would be no significant differences in AEs, serious AEs or AEs leading to treatment discontinuation.

6.40 A benefits and harms table was not presented for the delgocitinib vs dupilumab comparison as the submission made a claim of non-inferiority.

Clinical claim

6.41 The ESC considered that the therapeutic conclusion that delgocitinib demonstrated superior efficacy over SoC was supported by the evidence in the submission, with all primary and key secondary endpoints showing statistically significant improvements in favour of delgocitinib compared with SoC. However, the ESC noted that the comparative efficacy results should be interpreted in the context of the following limitations:

- The composition of SoC in the DELTA 1 and DELTA 2 trials (vehicle) was not reflective what would be received in clinical practice. For most patients who have

an intolerance to TCS or have failed to achieve satisfactory control with TCS, some degree of continuing TCS would be likely for symptom management.

- The main phase of the DELTA 1 and DELTA 2 trials was relatively short, lasting only 16 weeks, and the longer-term efficacy from DELTA 3 was an open label, uncontrolled trial.

6.42 The ESC considered that the claim of non-inferior safety of delgocitinib compared to SoC was reasonable, noting no emerging safety concerns and a low incidence of treatment-related AEs or SAEs. However, long-term safety remained uncertain.

6.43 The PBAC considered that the claim of superior comparative effectiveness to SoC was reasonable for the submission's definition of SoC, which included emollients and avoidance of irritants

6.44 The PBAC considered that the claim of non-inferior comparative safety to SoC was reasonable.

6.45 The submission described delgocitinib as non-inferior in terms of effectiveness compared to dupilumab. The ESC considered the claim of non-inferior efficacy was uncertain due to several differences between the pooled DELTA 1/2 and LIBERTY-AD-HAFT trials, which may have affected the transitivity of the trials (see paragraph 6.20). The ESC considered the Bucher indirect comparison presented in the PSCR did not add additional certainty to inform the claim of non-inferiority to dupilumab.

6.46 The submission made no safety claim for delgocitinib vs dupilumab.

6.47 The PBAC based on its view on the most appropriate place in therapy for delgocitinib and considered the claims versus dupilumab were not relevant.

Economic analysis

6.48 The submission presented a cost-utility analysis between delgocitinib and SoC and a cost-minimisation approach vs dupilumab.

Cost-utility analysis

6.49 Key components of the economic evaluation are given in Table 9.

Table 9: Summary of model structure, key inputs and rationale

Component	Summary
Type of analysis	Cost-utility analysis
Comparator	SoC (defined as non-medicated emollient use alone and avoidance of known irritants and allergens)
Outcomes	Life years gained, quality-adjusted life-years.
Time horizon	10 years in the model base case vs 16 weeks in the DELTA trials.
Methods used to generate results	Markov cohort model.
Health states	On treatment: full response (IGA-CHE 0 (Clear) or 1 (Almost clear)) On treatment: partial response (IGA-CHE 2 (Mild)) On treatment: low response (IGA-CHE 3 with 1-point improvement from baseline (Moderate)) On treatment: insufficient response (IGA-CHE 3 without improvement from baseline or IGA-CHE 4 (Severe)) Off treatment: full response (IGA-CHE 0 (Clear) or 1 (Almost clear)) Relapse: mild Relapse: moderate

Component	Summary
	Relapse: severe Permanent discontinuation: next-line treatment Permanent discontinuation: best supportive care (BSC). Death
Cycle length	4 weeks.
Mean starting age	44 years. Derived from DELTA 1 and DELTA 2 trials.
Severity of CHE	Moderate (IGA-CHE 3): 57.8% Severe (IGA-CHE 4): 42.2%. Derived from RWEAL.
Transition probabilities	Probability of full response at 12 weeks: Delgocitinib: 28.3%, SoC 11.1%. Derived from DELTA 1 and DELTA 2 trials. IGA-CHE severity state at 12 weeks: Delgocitinib: IGA-CHE 2 = 52.7%, IGA-CHE 3 = 38.5%, IGA-CHE 4 = 8.9%. SoC: IGA-CHE 2 = 28.1%, IGA-CHE 3 = 47.4%, IGA-CHE 4 = 24.5%. Derived from DELTA 1 and DELTA 2 trials. Per-cycle probability of full response with continued treatment by non-responder health state (partial response, low response and insufficient response): From partial response 10.5%, From low response 3.0%, From insufficient response: 0%. Derived from DELTA 3 trial. Per cycle probability of relapse: delgocitinib arm: 37% to mild, 20.9% to moderate, 2.2% to severe, SoC arm: 36.7% to mild, 20.9% moderate, 2.2% to severe. Delgocitinib arm values from DELTA FORCE trial, SoC arm values from DELTA 3 trial. Per-cycle probability of full response with re-treatment following relapse 20.2%, Derived from DELTA 3 trial. Per-cycle probability of discontinuation from initial treatment and re-treatment for delgocitinib: 2.8%[a]. Derived from DELTA FORCE trial. Per-cycle probability of opting-out from re-treatment for delgocitinib: 4.6%[b]. Derived from DELTA 3 trial. Probability of adverse event per cycle: Headache 0.67%, Nasopharyngitis 2.08%. Utility values associated with different levels of response were generated from pooled DELTA 1 and DELTA 2 trial results (see below). Probability that patients who discontinue first line treatment (delgocitinib) then move on to second line therapy (basket composition: emollients 100% of patients, TCS 99.2%, TCI 6.5%). From RWEAL study = 28%. Probability that patients who discontinue first line treatment (delgocitinib) then move on to best supportive care = 72%. Probability that patients receiving a basket of next-line treatments will have a full response at any given time = 40.6% Based on the RWEAL study.
Utilities	All utilities were from the DELTA 1 and DELTA 2 trials. Baseline: 0.672 Delgocitinib: Full response: 0.897 Partial response: 0.835 Low response: 0.748 Insufficient response: 0.659 SoC:

Component	Summary
	Full response: 0.873 Partial response: 0.811 Low response: 0.725 Insufficient response: 0.635 Second line: 0.808 Headache disutility: 0.038 Nasopharyngitis disutility: 0.038 BSC: equal to baseline
Costs	Amount applied per week of delgocitinib from DELTA 1, DELTA 2 and DELTA FORCE trials to achieve: Full response: 8.24 g Partial response: 8.75 g Low response: 8.78 g Insufficient response: 8.61 g EMP =$[redacted]; DPMQ = $[redacted] per 60g tube[c]. Costs of the following treatments in 2nd line therapy: Ciclosporin, Methotrexate, Acitretin, Azathioprine, Oral steroids, UVB, Dupilumab Weighted average per cycle cost of $340.03. Health state costs per model cycle: Full response $8.86 Partial and low response $29.19 Insufficient response $29.19 Second-line and third line treatment $20.94 BSC $29.19 Patients experiencing AEs were assumed to visit their general practitioner once at a cost of $42.85 (MBS item 23).
Software package	Microsoft Excel 365.

Source: Table 129, pp252-253, Table 131, p257, Table 133, p261, Table 134, p263, p270, Table 135, p265, Table 139, p270, Table 140, p272, Table 141, pp272-3, Table 142, p274, Table 143, p275, Table 146, p279, Table 149, p283, Table 156, p293 of the submission, economic model sheet IGA_breakdownBE, e_discontinuation.

AE = adverse event; BSC = best supportive care; CHE = chronic hand eczema; DPMQ = dispensed price for maximum quantity; EMP = ex-manufacturer price; IGA-CHE = Investigator's Global Assessment for chronic hand eczema; MBS = Medicare Benefits Schedule; NICE = National Institute for Health and Care Excellence; RWEAL = Real-World trEatment & mAnagement of chronic hand eczema in cLinical practice; SoC = standard of care; TCI = Topical calcineurin inhibitor; TCS = topical corticosteroids; UVB = Ultraviolet B.

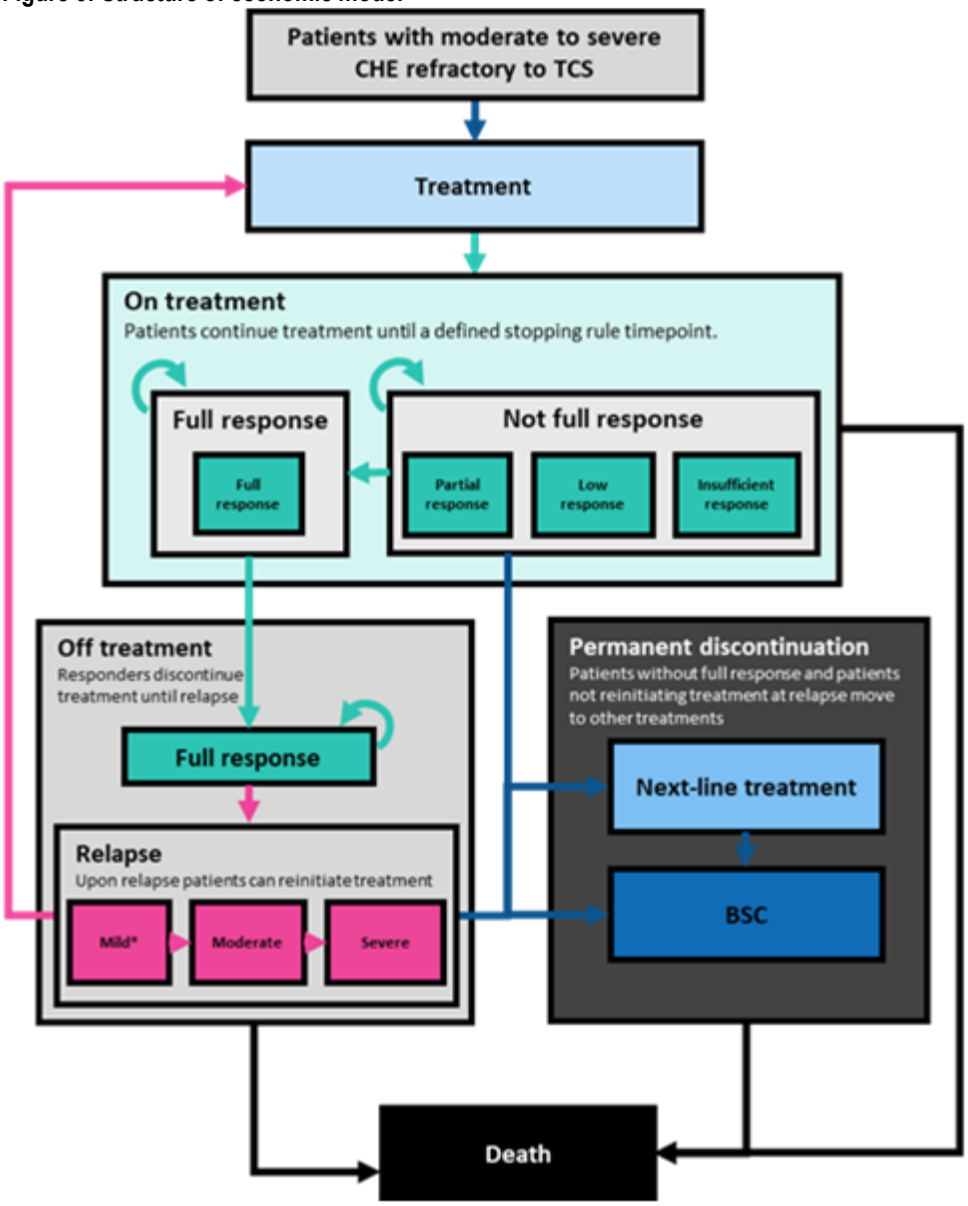
[a] Given as 2.8% in economic model and 1.4% in submission report (Table 139, p270).

[b] Given as 4.6% in economic model and 4.8% in submission report (Table 139, p270).

[c] The DPMQ applied in the model differed slightly from that proposed in the submission of $[redacted] (using July 2025 mark-ups)

6.50 The model structure is presented in Figure 3. The ESC considered the model structure may be unnecessarily complicated but acknowledged a model with the same structure was included in the submission to NICE.

Figure 3: Structure of economic model



Source: Figure 47, p255 of the submission
BSC; best supportive care; CHE; chronic hand eczema; TCS; topical corticosteroids.
Note: Re-initiation of treatment at partial response is applicable to delgocitinib only

6.51 In the base case analysis, treatment was assumed to continue for the first 12 weeks. During this period, patients started in a baseline state and could transition to full response during any cycle.

6.52 Full response was defined as an IGA-CHE TS score of 0 or 1, partial response was a score of 2, low response was a score of 3 with a 1-point improvement, and insufficient response was a score of 4 or a score of 3 without a 1-point improvement. IGA-CHE TS score was the primary outcome of the DELTA 1 and DELTA 2 trials. A sensitivity analysis using the secondary outcome of HECSI 90 was presented in the submission. Patients were assumed to discontinue treatment after achieving full response. Given the

relapsing-remitting nature of CHE, relapses are a key component of the condition and were reflected in the economic model. Relapse was defined as the transition from a full responder off-treatment to an IGA-CHE ≥ 2. A transition from full response to a mild state (IGA-CHE 2) was described as a loss of response, whilst a transition to a moderate or severe state (IGA-CHE 3 or 4) was described as a relapse.

6.53 At Week 12, patients not yet in full response were distributed across three other on treatment health states, partial, low and insufficient, based on data from the DELTA trials. Patients who had not yet achieved full response (i.e. those in the partial or low response states) by Week 12 could continue treatment and go on to achieve full response at a later timepoint. Evidence from a *post-hoc* analysis of the DELTA 3 trial indicated that partial/low responders might achieve full response with further delgocitinib therapy. Patients with an insufficient response discontinued treatment at Week 12. However, as the proposed restriction did not include a stopping rule, the assumption implicitly relies on clinical practice occurring in a specific way that is not bound by the restriction.

6.54 After ceasing initial treatment, patients could relapse to mild, moderate or severe CHE and could recommence delgocitinib. Relapsing patients who did not achieve full response discontinued delgocitinib and moved to next-line treatment or best supportive care (BSC).

6.55 Patients who discontinued, after not responding or for any other reason, moved on to next-line therapy or BSC.

6.56 Whilst the ESC considered that a 10 year time horizon was long compared to the 16 week comparative data, it noted that all patients had discontinued delgocitinib treatment by 5 years.

6.57 The percentage of patients remaining on treatment with delgocitinib at 2 years was approximately 6% (i.e. those in the partial and low response health states). The evaluation considered that the mean treatment duration of delgocitinib was potentially underestimated. The ICER was sensitive to the proportion of patients remaining on treatment. If treatment duration increases, it is possible that QALYs in the delgocitinib arm would also increase. However, assuming no such change in QALYs and increasing the proportion of patients remaining on treatment at 2 years to 25%, increased the ICER from $45,000 to < $55,000 to $95,000 to < $115,000 per QALY gained. Overall, the ESC considered the assumption that 6% of patients could continue receiving treatment at 2 years was implausibly low but accepted that 25% may not be an appropriate alternative input. The Pre-PBAC Response stated that assumptions of increased continuous use of delgocitinib without considering a commensurate gain in QALYs were implausible and overly conservative.

6.58 For each response health state, the submission applied a treatment effect utility benefit to patients receiving delgocitinib of 0.024. However, for any given health state, it was not clear what benefit delgocitinib had over SoC. Assuming no treatment effect increased the ICER from $45,000 to < $55,000 to $45,000 to < $55,000 per QALY gained. The PSCR stated that delgocitinib demonstrated a statistically significant

benefit in health-related quality of life in the clinical trials over vehicle (DELTA 1/2) and that in the context of the observed benefit, it would be implausible to assume delgocitinib provides no utility benefit. The ESC considered the addition of a treatment specific utility benefit for delgocitinib in addition to the benefit associated with responding to treatment to be inadequately supported. The Pre-PBAC Response stated that a statistically significant effect on EQ-5D improvement was observed in the trials, and the Week 16 change was modelled as a function of age, baseline utility, HECSI, symptom diary, pain score and treatment received, and the results demonstrated a strong effect that could not be fully explained by the health states and other parameters. The pre-PBAC Response also stated that the approach preferred by the ESC of setting the delgocitinib utility gains to be the same as vehicle introduces inappropriate bias by excluding delgocitinib patients from the analysis.

6.59 The submission assumed no wastage of delgocitinib. Assuming wastage of half a tube of delgocitinib for all patients increased the ICER from $45,000 to < $55,000 to $45,000 to < $55,000 per QALY gained. The ESC considered it was appropriate for some wastage to be considered in the model.

6.60 Key drivers of the economic model are given in Table 10.

Table 10: Key drivers of the model

Description	Method/Value	Impact Base case: $[redacted][1]/QALY gained
Time on delgocitinib treatment	The percentage of patients continuing to receive treatment with delgocitinib at 2 years was approximately 6%.	High impact, likely favours delgocitinib.
Extent of wastage of delgocitinib	No wastage of delgocitinib assumed.	Moderate impact, favours delgocitinib. Assuming wastage of half a tube of delgocitinib increased the ICER to $[redacted][1] per QALY.
Utilities	For each response health state there was a utility treatment effect of delgocitinib vs SoC of 0.024. For any given health state, it was not clear what benefit delgocitinib had over SoC in addition to response.	Moderate impact, favours delgocitinib. Assuming no treatment specific utilities, the ICER increased $[redacted][1] to $[redacted][1] per QALY.

Source: Table 148, pp280-2 of the submission, Table 158, p299 of the submission.
AEMP = Approved Ex-Manufacturer Price; DPMQ = dispensed price for maximum quantity; ICER = incremental cost-effectiveness ratio; NICE = National Institute of Health and Care Excellence, SOC = Standard of care; QALY = quality-adjusted life-year.
The redacted values correspond to the following ranges:
[1] $45,000 to < $55,000

6.61 The base case results, using the DPMQ for delgocitinib, are given in Table 11. The submission did not present a stepped evaluation.

Table 11: Results of the economic evaluation

Component	Delgocitinib	Standard of care	Increment
Discounted Costs	$[redacted]	$5,850	$[redacted]
Discounted QALYs	5.327	5.243	0.083
Incremental cost/extra QALY gained			**$[redacted][1]**

Source: Adapted from Table 155, p292 of the submission.
QALY = quality adjusted life year.
The redacted values correspond to the following ranges:
[1] $45,000 to < $55,000

6.62 The results of key sensitivity analyses are summarised in Table 12.

Table 12: Sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER	% change to ICER
Base case	**$[redacted]**	**0.083**	**$[redacted][1]**	**-**
Discount rate 0% (base case: 5%)	$[redacted]	0.090	$[redacted][1]	-[redacted]%
Discount rate 3.5% (base case: 5%)	$[redacted]	0.085	$[redacted][1]	-[redacted]%
Response is defined as HECSI 90 (base case: IGA-CHE)	$[redacted]	0.095	$[redacted][2]	-[redacted]%
Time horizon reduced from 10 to 3 years	$[redacted]	0.074	$[redacted][1]	[redacted]%
Data is extracted at Week 16 endpoint from the DELTA 1 and DELTA 2 trials (base case: Week 12 endpoint)	$[redacted]	0.075	$[redacted][1]	[redacted]%
Health state utilities are treatment independent, i.e. equal to vehicle treatment arm (base case: 0.024 utility benefit applied to each health state for delgocitinib patients)	$[redacted]	0.079	$[redacted][1]	[redacted]%
Increase the total usage of delgocitinib by a factor of 2.06 to yield percentage of people continuing to receive treatment with delgocitinib at 2 years in the model of 25%. (base case: 6% continuing to receive treatment at 2 years)	$[redacted]	0.083	$[redacted][3]	[redacted]%
Increase the total usage of delgocitinib by a factor of 1.05 to yield percentage of people continuing to receive treatment with delgocitinib at 2 years in the model of 15%. (base case: 6% continuing to receive treatment at 2 years)	$[redacted]	0.083	$[redacted][4]	[redacted]%
Allow for wastage of: - 50% of a tube of delgocitinib - 25% of a tube of delgocitinib	 $[redacted] $[redacted]	 0.083 0.083	 $[redacted][1] $[redacted][1]	 [redacted]% [redacted]%
Per-cycle probability of full response with re-treatment following relapse = 10% (base case: 20.2%)	$[redacted]	0.058	$[redacted][4]	[redacted]%
HRQoL in BSC assumed equal to vehicle arm of the DELTA 1/DELTA 2 trials at Week 12 (0.72) (base case: 0.672)	$[redacted]	0.058	$[redacted][4]	[redacted]%

Source: Economic model of the submission.

AEMP = approved ex-manufacturer price; BSC = best supportive care; DPMQ = dispensed price for maximum quantity; HECSI; hand eczema severity index; HRQoL = health-related quality of life; ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year.

The redacted values correspond to the following ranges:

[1] *$45,000 to < $55,000*

[2] *$35,000 to < $45,000*

[3] *$95,000 to < $115,000*

[4] *$55,000 to < $75,000*

6.63 Given its view on the most appropriate place in therapy and comparator(s) for delgocitinib (see paragraphs 4.6 and 5.3), the ESC considered the model was only useful if the proposed place in therapy was accepted. If the proposed place in therapy was not accepted by the PBAC, a new economic modelling approach would be required.

6.64 The PBAC considered the economic evaluation provided in the submission was not reliable for decision-making. The PBAC considered a trial-based analyses using the EQ-5D-5L index scores and extent of use of delgocitinib from the DELTA 1 and DELTA 2 trials to be informative. The EQ-5D-5L results are presented in Table 13. The PBAC noted that an alternative approach of assuming a linear trend between time points would result in as slightly smaller QALY gain over 16 weeks.

Table 13: Change in mean EQ-5D-5L index score from baseline by visit

	DELTA 1 (N = 479)				DELTA 2 (N = 469)			
	Delgocitinib	Vehicle	Difference	Utility difference per period	Delgocitinib	Vehicle	Difference	Utility difference per period
Week 1	0.091	0.037	0.054	0.00104	0.071	0.070	0.000	0.00000
Week 4	0.142	0.063	0.079	0.00456	0.139	0.064	0.075	0.00433
Week 8	0.172	0.083	0.089	0.00685	0.149	0.059	0.090	0.00692
Week 12	0.171	0.078	0.093	0.00715	0.151	0.044	0.107	0.00823
Week 16	0.176	0.073	0.103	0.00792	0.157	0.049	0.108	0.00831
Total per 16 weeks				0.02752				0.02781
Weighted QALY gain over 16 weeks	0.02766							

Source: Table 2.7.2, p470 of the DELTA 1 CSR and Table 2.7.2, p474 of the DELTA 2 CSR

6.65 Noting the differences between patients and the responses in the trials, the PBAC considered that using a weighted QALY gain would be reasonable. The PBAC noted that patients in the DELTA 1 and DELTA 2 trials used a mean of 133 g and 120 g, respectively, of delgocitinib over 16 weeks, resulting in a weighted average of 126.6 g.

Table 14: Trial based economic analysis based on 16 weeks of delgocitinib use

	Use of delgocitinib	Cost per 60 g tube	Total cost over 16 weeks	QALY gain	ICER
No wastage	126.6 g	$[redacted]	$[redacted]	0.02766	$[redacted][1]
+ 25% wastage	158.2 g		$[redacted]		$[redacted][2]
+ 33% wastage	168.3 g		$[redacted]		$[redacted][2]
+ 50% wastage[a]	189.9 g		$[redacted]		$[redacted][3]

Source: Created during PBAC consideration

ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year

[a] Based on sensitivity analyses in the pre-PBAC response which included 50% wastage

The redacted values correspond to the following ranges:

[1] *$55,000 to < $75,000*

[2] *$75,000 to < $95,000*

[3] *$95,000 to < $115,000*

Cost-minimisation approach

6.66 The submission also presented a cost-minimisation approach vs dupilumab.

6.67 The evaluation considered a cost minimisation approach may not be reasonable as the claim of non-inferior efficacy between delgocitinib and dupilumab was uncertain and no claim regarding safety was presented. The ESC and PBAC considered the CMA to dupilumab was not informative for determining a cost effective price as (i) it is unclear whether dupilumab will be replaced in clinical practice, (ii) such a comparison is only relevant to the atopic subtype and (iii) there was substantial uncertainty in the clinical comparison that meant the clinical claim of non-inferior comparative effectiveness was not adequately supported. Therefore, further detail on the proposed CMA is not presented.

Drug cost/patient/course

6.68 The drug cost per patient per course is given in Table 15.

Table 15: Drug cost per patient for delgocitinib

	Delgocitinib Trial dose and duration	Delgocitinib Model	Delgocitinib Financial estimates
Mean dose	DELTA 1 weekly dose 8.54 g DELTA 2 weekly dose 7.72 g	Weekly dose to obtain: Full response: 8.24 g Partial response: 8.75 g Low response: 8.78 g Insufficient response: 8.61 g	
Mean duration	DELTA 1: 3.6 months[a] DELTA 2: 3.6 months[a]	6.94 months[db]	
Cost/patient/month	-	$ [redacted]	
Cost/patient/course	-	$ [redacted]	

[a] Table 74, p127 of the submission. Note, DELTA 1 and DELTA 2 had a duration of 16 weeks.

[b] Calculated from data in Delgo_Engine worksheet of the economic model and included patients who had either had a full response and ceased or had responded and restarted treatment, those with a partial or low response who continued treatment, and those who had an insufficient response and ceased treatment

Estimated PBS usage & financial implications

6.69 This submission was not considered by DUSC. The submission used an epidemiological approach to estimate the utilisation of delgocitinib.

6.70 Key inputs for financial estimates are given in Table 16.

Table 16: Key inputs for financial estimates

Data	Value	Source	Comment
Eligible population			
Australian population by year, with growth included	Aged ≥18 to 90 years	ABS population 3222.0 Series B	It is not clear why patients aged >90 years were excluded. Additionally, although limiting the patient population to adults only aligns with the proposed TGA indication, it does not align with the proposed PBS restriction which was age agnostic.
Pooled incidence HE in adults	7.5 cases/1000 person-years (95% CI: 5.2, 9.5)	Quaade 2021	The source did not include Australian data (only included European studies).
Proportion of HE that is CHE based on definition used in this submission	52.2%	CHECK Study Final Report	-
12-month prevalence of CHE	4.7% (95% CI: 4.5, 4.9)	Apfelbacher 2025 Voorberg 2022	-
Proportion of moderate to severe CHE patients using TCS-only	22.2%	CHECK Study Final Report Table 53, page 77	The proportion of participants was 21.7%, rather than 22.2%. However, this had a minimal effect on the results.
Proportion of moderate to severe CHE patients with an inadequate response to TCS or contraindicated to TCS, %	41.3%	Census population[a] RWEAL Study Final Report	-
Uptake			
Proportion of eligible patients prescribed treatment with delgocitinib	Years 1 to 6: [redacted]%	Expert opinion	-
Initial treatment			
Duration of treatment	12 weeks	Proposed Australian PI	-

Data	Value	Source	Comment
Proportion by response type[b] within initial treatment period: Full response Partial response Low response Insufficient response	 28.3% 37.8% 10.0% 23.9%	Pooled DELTA 1 and DELTA 2 trials.	-
Compliance rate in initial treatment period (100% minus days missed)	81.66%	DELTA 1 and DELTA 2 trials	The data could not be verified; however, it is likely to be an overestimate due to clinical trial population and conditions.
Continuing treatment – compliance assumed as per initial treatment period			
Continuing treatment based upon initial response Full response Partial or low response Insufficient response	Patients cease treatment and remain at risk of recurrence/ exacerbation. 47.8% of patients continue treatment for up to a further 12 weeks. Patients cease treatment.	DELTA 1 and DELTA 2 trials 47.8% is derived from partial response (37.8%) plus low response (10%) values above.	-
Drug costs			
Delgocitinib 20 mg/g cream, 60-gram tube	Effective DPMQ = $[redacted][c]	Submission	-

Source: Table 163, pp311-313 of the submission.
ABS, Australian Bureau of Statistics; ATC = Anatomical Therapeutic Chemical, CHE = chronic hand eczema; CSR = clinical study report; DPMQ = dispensed price for maximum quantity; HE = hand eczema; TCS = topical corticosteroid.
[a] RWEAL Study criteria for inclusion in the census population were: Adult patients aged 18 years or over; Patients with moderate to severe CHE at the time of the last visit; and Patients seen in consultation by the physician in the past 12 months prior to the enrolment date. Additional patient criteria for inclusion in the focus population were patients who had been treated with TCS, in combination or not with other CHE treatments, in the 12 months prior to the last visit, or for whom TCS were contraindicated.
[b] Full response (IGA-CHE score 0/1 TS); Partial response (IGA-CHE score 2); Low response (IGA-CHE score 3, with 1-point improvement from baseline); Insufficient response (IGA-CHE 3 without improvement from baseline or IGA-CHE 4
[c] The price applied in the financial model differed slightly from that proposed in the submission ($[redacted] using July 2025 mark-ups)

6.71 The estimated use and financial implications of listing delgocitinib are given in Table 17.

Table 17: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of delgocitinib use						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Number of scripts dispensed	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][4]
Estimated financial implications of delgocitinib						
Cost to PBS/RPBS less copayments	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][6]	$[redacted][6]
Estimated financial implications for standard of care						
Cost to PBS/RPBS less copayments	$0	$0	$0	$0	$0	$0
Net financial implications						
Net cost to PBS/RPBS	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][6]	$[redacted][6]
Net cost to MBS/Services Australia/other	$0	$0	$0	$0	$0	$0
Net cost to PBS/RPBS/MBS/ Services Australia	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][6]	$[redacted][6]

Source: Table 164, p316 and Table 168, p321 of the submission. Only evaluation-corrected figures presented.
MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme, RPBS = Repatriation Pharmaceutical Benefits Scheme *The redacted values correspond to the following ranges:*
[1] *5,000 to < 10,000*
[2] *10,000 to < 20,000*
[3] *20,000 to < 30,000*
[4] *30,000 to < 40,000*
[5] *$10 million to < $20 million*
[6] *$20 million to < $30 million*

6.72 The total cost to the PBS/RPBS of listing delgocitinib was estimated to be $20 million to < $30 million in Year 6, and total $100 million to < $200 million over the first 6 years of listing.

6.73 The submission assumed no displacement or replacement of dupilumab or other subsequent treatments by delgocitinib. The ESC considered that the replacement of dupilumab was likely to be relatively small.

6.74 The ESC considered a number of inputs to the model, including duration of treatment, were uncertain and could be highly impactful to the likely overall cost of delgocitinib. The ESC also considered there was a substantial risk of greater than expected use due to use on other body areas. The Pre-PBAC Response stated that the utilisation estimates would be limited in practice by access to dermatologists to prescribe delgocitinib.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended the General Schedule, Authority Required (telephone/electronic) listing of delgocitinib cream formulation for the treatment of moderate to severe chronic hand eczema (CHE), in patients who have previously not adequately responded to ongoing treatment with medium to high potency topical corticosteroids (TCS), or where eczema has repeatedly recurred, or for patients who are contraindicated to TCS. In making this recommendation, the PBAC considered

delgocitinib should be available for prescribing by medical practitioners, with flexibility to allow for clinical decision-making in terms of patient age and potential combination therapy with other treatments, but with limits on the quantity of delgocitinib to be dispensed to ensure use is limited to CHE and not eczema on other body areas. The PBAC was satisfied that delgocitinib provides, for some patients, a significant improvement in efficacy over vehicle (representing standard of care; SoC), and has a clinical place after inadequate response to high dose TCS. The PBAC considered that the economic model was not useful for decision-making as it was based on multiple treatment cycles for which there was no comparative data, it was unclear if the modelled treatment duration reflected that expected in clinical practice and there were applicability concerns regarding the use of standard of care (SoC) as the comparator. Instead, given the likely episodic nature of delgocitinib use for most patients and the availability of utility values from the comparative trials, the PBAC considered that a trial based economic analysis using the utility values and delgocitinib use over 16 weeks was a reasonable basis for assessing cost effectiveness. Based on this approach, the PBAC considered delgocitinib would be acceptably cost effective with a reduced price.

7.2 The PBAC acknowledged CHE is a debilitating form of dermatitis that has a particular impact for patients and that in more severe cases it can be painful, impede daily activities, and the ability to work and function in society. The PBAC acknowledged there is a clinical need for additional effective therapies, as many patients with CHE have repeatedly recurring disease, have used TCS long-term with inadequate effect or may have contraindications to TCS. The PBAC acknowledged that a therapeutic gap exists as patients have limited alternative topical treatments, as well as limited acceptable systemic treatments given immunosuppressants have known safety issues, and the use of biologics or targeted therapies (dupilumab or upadacitinib) are restricted on the PBS to the atopic subtype with severe symptoms. The PBAC noted that phototherapy may also be used, but that access was limited. The PBAC also recalled it had recommended tacrolimus cream (a TCI) for atopic dermatitis in July 2025 for use in the first line setting, but that at time of consideration of delgocitinib it had not progressed to a listing.

7.3 The PBAC provided advice regarding the restriction, suggesting that it should:

- Allow prescribing by medical practitioners of any kind (noting that although the submission had requested restricting to or in consultation with a dermatologist, there were known issues accessing dermatologists);
- Include limitations on the quantity dispensed and the number of repeats to ensure PBS subsidy is limited to quantities necessary to treat CHE only, not other body areas;
- Have an initial 12 week treatment phase restriction. Patients who presented an insufficient response (based on the IGA – CHE scoring system) would no longer be able to access PBS-subsidised delgocitinib treatment (i.e. a stopping rule). However, patients who presented a partial or low response would be able to

access therapy under the 'Additional 12 weeks in a treatment course' treatment phase;

- Have both treatment phases as Authority Required (telephone/electronic) listings;
- Clearly outline that patients should take a break in treatment and reinitiate only if there is an active flare-up of their CHE;
- Continue to require an assessment of moderate-to-severe CHE with an investigator's global assessment of CHE (IGA-CHE) score of 3 or 4 that has lasted for more than 3 months prior to initiating their most recent course of PBS-subsidised treatment with this drug;
- Allow patients to retrial therapy with delgocitinib, if they have experienced a flare up that has returned twice or more within the last 12 months;
- Include the wording 'medium to high potency' in relation to topical corticosteroid therapy and ensure that patients only need to present that they were unable to respond to topical corticosteroid therapy prior to receiving their first PBS-subsidised treatment with this drug for this condition. This will ensure patients who are experiencing a flare-up will not need to cease delgocitinib and retrial topical corticosteroid therapy again for 12 months, in order to access further treatment with PBS-subsidised delgocitinib.
- Be age agnostic; and
- Not include a requirement for treatment to be as monotherapy.

7.4 The PBAC noted that the submission did not propose a grandfather restriction. The PBAC noted that wording to accommodate for patients wishing to transition from non-PBS subsidised to PBS subsidised treatment may be required at the time of the PBS listing of delgocitinib.

7.5 The PBAC noted that flow-on restriction changes would be required for dupilumab and upadacitinib, for use in patients aged 12 years or older, to allow use following treatment with delgocitinib after confirmation of a diagnosis of chronic, severe atopic dermatitis of the hand.

7.6 The Committee noted the submission requested a second line listing for patients who had failed prior treatment with TCS, or for patients who are contraindicated or are intolerant to TCS, but prior to systemic or targeted therapies, and nominated SoC, consisting of non-medicated emollients and avoidance of known irritants, as the main comparator. The PBAC considered that the make-up of SoC, as defined in the submission, did not reflect the treatments likely to be replaced in practice, and that at least a proportion of patients would be receiving TCS (see paragraph 7.2). However, noting that clinical evidence against TCS was unlikely to become available, the PBAC accepted the comparison versus SoC. The PBAC noted that dupilumab was proposed by the submission as a secondary comparator, but considered that this was not appropriate as, although there may be some displacement of dupilumab in a proportion of patients with the atopic subtype, the extent of replacement was likely to be small.

7.7 The PBAC noted the submission was supported primarily by two randomised

controlled trials (DELTA 1 and DELTA 2) comparing delgocitinib over 16 weeks, as monotherapy, compared with vehicle in patients in whom TCS was ineffective or inappropriate, and the open label extension study of these trials (DELTA 3).

7.8 The PBAC noted that the pooled results of the DELTA 1 and DELTA 2 trials found delgocitinib was associated with a statistically significantly higher chance of achieving IGA-CHE treatment success, with a 24.3% responder rate for delgocitinib and 8.4% for vehicle (risk difference (RD) 15.9%, 95% CI 11.4, 20.4). Additionally, there were statistically significant differences favouring delgocitinib in both the DELTA 1 and DELTA 2 trials for secondary outcomes including HECSI-75 and -90, HESD itch and pain reduction health-related quality of life (HRQoL) outcomes including DLQI and EQ-5D-5L index scores (treatment difference = 0.103; 95% CI: 0.067, 0.140 in DELTA 1 and treatment difference = 0.108; 95% CI: 0.071, 0.145 in DELTA 2). The Committee noted subgroup analyses by CHE subtype, as well as the results of the DELTA-3 open label extension (OLE) study, indicated some variation in response between subtypes but acknowledged the results generally favoured delgocitinib (see paragraphs 6.27 and 6.28). Overall, the PBAC considered delgocitinib was superior in terms of comparative effectiveness compared to vehicle.

7.9 The PBAC noted the safety data reported in DELTA 1, DELTA 2 and DELTA 3 OLE found delgocitinib had a comparable safety profile to vehicle. Delgocitinib was well-tolerated and there were no emerging safety concerns observed up to 36 weeks.

7.10 The PBAC considered the economic evaluation as presented was not reliable for decision making. The PBAC noted the model assessed multiple treatment cycles with delgocitinib; however, there was comparative clinical evidence for only one treatment cycle, and considerable uncertainty regarding the likely duration over which delgocitinib would be used. The PBAC noted that in the model at 2 years only 6% of patients continued to receive delgocitinib (i.e. they were in the 'partial' or 'low response' health states) with an additional 4% of patients eligible for a subsequent course of delgocitinib treatment (i.e. in the 'full response' health state). The remaining 90% of patients either had 'insufficient response' or were treated with 'next line treatment or BSC' (or were dead) and unable to be re-treated with delgocitinib (see Figure 3). The PBAC considered this likely underestimated the duration over which delgocitinib would be used in clinical practice.

7.11 In the context of utility values being available directly from the DELTA 1 and DELTA 2 trials (collected using the EQ-5D-5L), the PBAC considered a trial-based analysis using the weighted utility values and cost of delgocitinib to be a reasonable approach for assessing cost-effectiveness (see

7.12 Table 14). The PBAC noted the resulting ICER approximately $55,000 to < $75,000 per QALY gained assuming no wastage with delgocitinib. Noting patients will cease treatment when the skin is clear or almost clear, the PBAC considered there will likely be substantial wastage. The PBAC noted the ICER increased to approximately $75,000 to < $95,000 per QALY gained assuming 25% wastage and to $75,000 to < $95,000 per

QALY gained assuming 33% wastage. The PBAC considered these ICERs unacceptably high. In the context of the simplified approach, the unknown cost-effectiveness of delgocitinib when used beyond 16 weeks and over more than one treatment cycle, and applicability concerns regarding SOC as defined above, the PBAC considered delgocitinib would be cost-effective if the ICER was less than $5,000 to < $15,000 per QALY[7] gained for the scenario which assumed 25% wastage.

7.13 The PBAC considered the utilisation estimates to be reasonable. The PBAC noted that there were uncertainties arising from how delgocitinib may be used in practice, the extent to which it would replace other active topical treatments, uptake, how it would be used in patients who achieve a partial response, risk of use in other body areas and level of wastage; however, considered that the Authority level and the restrictions applied to the amount allowed to be prescribed would contain use. The PBAC advised that the utilisation of delgocitinib should be reviewed 24 months after listing.

7.14 The PBAC advised that the Early Supply Rule should not apply as it cannot currently be applied extemporaneous preparations listings.

7.15 The PBAC recommended that delgocitinib should not be treated as interchangeable with any other drugs.

7.16 The PBAC advised that delgocitinib is not suitable for prescribing by nurse practitioners.

7.17 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for delgocitinib:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, over alternative therapies, as other topical treatments are available and can be used as second-line therapies, and the comparative effectiveness of delgocitinib to these treatments is not known;

b) The treatment is not expected to address a high and urgent unmet clinical need as other treatments are available, including systemic and targeted immunosuppressants (under certain circumstances) for when current topical therapies are not effective;

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

7.18 The PBAC noted that this submission is not eligible for an Independent Review as it

[7] The PBAC is open to receiving new evidence that may support changes to its recommendations. The sponsor has submitted further information for future PBAC consideration, which it believes would be relevant to the PBAC's consideration of the ICER.

received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DELGOCITINIB						
Delgocitinib 20 mg / g (2%) cream 60 g tube		NEW MP	1	1	2	Anzupgo
Restriction Summary NEW 1 / Treatment of Concept: NEW 1A						
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)					
	Prescriber type: ☒ Medical Practitioners					
	Restriction type: ☒ Authority Required (immediate assessment) – telephone/electronic via Online PBS Authorities					
Prescribing rule level	**Administrative Advice:** No increase in the maximum quantity or number of units may be authorised.					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.					
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.					
	Episodicity: Chronic					
	Severity: moderate to severe					
	Condition: Chronic hand eczema					
	Indication: moderate to severe chronic hand eczema (CHE)					
	Treatment phase: Initial 12 weeks treatment course					
	Clinical criteria:					
	Patient must have moderate to severe chronic hand eczema with an Investigator Global Assessment-Chronic Hand Eczema (IGA-CHE) score of 3 or 4, that has lasted for more than 3 months prior to initiating their most recent course of PBS-subsidised treatment with this drug					
	OR					
	Patient must be experiencing a flare-up, that has returned twice or more within the last 12 months prior to initiating their most recent course of PBS-subsidised treatment with this drug					
	AND					
	Clinical criteria:					
	Patient must have failed to respond to daily topical corticosteroids of medium to high potency in the 12 months prior to receiving their first PBS-subsidised treatment with this drug for this condition					
	OR					
	Patient must be contraindicated for treatment with daily topical corticosteroids of medium to high potency					

	Prescribing Instructions: The IGA-CHE scores are defined as: (i) Full response – IGA-CHE 0 (Clear) or 1 (Almost clear) (ii) Partial response – IGA-CHE 2 (Mild) (iii) Low response – IGA-CHE 3 with 1-point improvement from baseline (Moderate) (iv) Insufficient response – IGA-CHE 3 without improvement from baseline, or IGA-CHE 4 (Severe) Once a full response is achieved, patients should take a break in delgocitinib treatment and reinitiate only if there is a flare-up of their CHE.
	Administrative advice: Moderate to severe chronic hand eczema is defined as IGA-CHE score of 3 or 4
	Administrative advice: Failure to achieve an adequate response to topical medium to higher potency corticosteroids is defined as failure to achieve IGA-CHE score of ≤ 2 despite daily use.
Restriction Summary NEW 2 / Treatment of Concept: NEW 2A	
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Restriction type: ☒ Authority Required (immediate assessment) – telephone/electronic via Online PBS Authorities
Prescribing rule level	**Administrative Advice:** No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Episodicity: Chronic
	Severity: moderate to severe
	Condition: Chronic hand eczema
	Indication: moderate to severe chronic hand eczema (CHE)
	Treatment phase: Additional 12 weeks in a treatment course
	Clinical criteria:
	Patient must be both of: (i) received the Initial PBS-subsidised 12-week treatment course with this drug (ii) have demonstrated a partial/low response to delgocitinib
	Prescribing Instructions: The IGA-CHE scores are defined as: (i) Full response – IGA-CHE 0 (Clear) or 1 (Almost clear) (ii) Partial response – IGA-CHE 2 (Mild) (iii) Low response – IGA-CHE 3 with 1-point improvement from baseline (Moderate) (iv) Insufficient response – IGA-CHE 3 without improvement from baseline, or IGA-CHE 4 (Severe) Once a full response is achieved, patients should take a break in delgocitinib treatment and reinitiate only if there is a flare-up of their CHE.
	Prescribing instructions: Treatment should be discontinued, and further treatment options should be considered if a full response is not achieved (IGA-CHE or 0 or 1) after a total of 24 weeks of continuous treatment Once a full response is achieved, patients should take a break in delgocitinib treatment and reinitiate only if there is a flare-up of their CHE.

8.2 Flow on changes to dupilumab listings:

Chronic severe atopic dermatitis (12 years of age or older population)

Treatment Phase: Initial treatment of the face and/or hands
15035H, 12291X, 14979J, 12292Y

Restriction Summary 17015 / Treatment of Concept: 17076	
Replace concept ID 27508:	With new Concept ID:
The condition must have at least 2 of the following Eczema Area and Severity Index (EASI) symptom sub-scores for erythema, oedema/papulation, excoriation, lichenification rated as severe despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days; or	The condition must have at least 2 of the following Eczema Area and Severity Index (EASI) symptom sub-scores for erythema, oedema/papulation, excoriation, lichenification rated as severe despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor/ *topical JAK inhibitor*), for at least 28 days; or
Replace concept ID 27059:	With new Concept ID:
The condition must have affected at least 30% of the face/hands surface area despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days	The condition must have affected at least 30% of the face/hands surface area despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor/ *topical JAK inhibitor*), for at least 28 days
Replace concept ID 27056:	With new Concept ID:
Patient must have an age appropriate Dermatology Life Quality Index (DLQI) baseline score (of any value) measured following treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days	Patient must have an age appropriate Dermatology Life Quality Index (DLQI) baseline score (of any value) measured following treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor/ *topical JAK inhibitor*), for at least 28 days
Replace concept ID 28253:	With New PI:
Prescribing Instructions: State each of the 4 Eczema Area and Severity Index (EASI) symptom sub-score ratings (0 = none, 1 = mild, 2 = moderate, 3 = severe) for: (i) erythema, (ii) oedema/papulation, (iii) excoriation, (iv) lichenification Acceptable scores can be: (a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication. State the percentage face/hand surface area affected by the condition (must be at least 30%) where EASI symptom sub-scores are not provided. This percentage surface area can also be stated in addition to the EASI symptom sub-scores. The EASI/percentage surface area and DLQI baseline measurements are to form the basis of determining if an adequate response to treatment has been achieved under the Continuing treatment restriction. In addition to stating them in this authority application, document them in the patient's medical records. Document the details of the medium to high potency topical corticosteroids (or calcineurin inhibitors) initially trialled are in the patient's medical records.	**Prescribing Instructions:** State each of the 4 Eczema Area and Severity Index (EASI) symptom sub-score ratings (0 = none, 1 = mild, 2 = moderate, 3 = severe) for: (i) erythema, (ii) oedema/papulation, (iii) excoriation, (iv) lichenification Acceptable scores can be: (a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication. State the percentage face/hand surface area affected by the condition (must be at least 30%) where EASI symptom sub-scores are not provided. This percentage surface area can also be stated in addition to the EASI symptom sub-scores. The EASI/percentage surface area and DLQI baseline measurements are to form the basis of determining if an adequate response to treatment has been achieved under the Continuing treatment restriction. In addition to stating them in this authority application, document them in the patient's medical records. Document the details of the medium to high potency topical corticosteroids (or / calcineurin inhibitors/*JAK inhibitors*) initially trialled are in the patient's medical records.

8.3 Flow on changes to upadacitinib listings:

Chronic severe atopic dermatitis
Treatment Phase: Initial treatment of the face and/or hands (12 years of age or older population)

12828E, 12836N

Restriction Summary 12508 / Treatment of Concept: 12508	
Replace concept ID 27058:	With new Concept ID:
The condition must have at least 2 of the following Eczema Area and Severity Index (EASI) symptom sub-scores for erythema, oedema/papulation, excoriation, lichenification rated as severe despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days; or	The condition must have at least 2 of the following Eczema Area and Severity Index (EASI) symptom sub-scores for erythema, oedema/papulation, excoriation, lichenification rated as severe despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor/ *topical JAK inhibitor*), for at least 28 days; or
Replace concept ID 27059:	With new Concept ID:
The condition must have affected at least 30% of the face/hands surface area despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days	The condition must have affected at least 30% of the face/hands surface area despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor/ *topical JAK inhibitor*), for at least 28 days
Replace concept ID 27056:	With new Concept ID:
Patient must have an age appropriate Dermatology Life Quality Index (DLQI) baseline score (of any value) measured following treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days	Patient must have an age appropriate Dermatology Life Quality Index (DLQI) baseline score (of any value) measured following treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor/ *topical JAK inhibitor*), for at least 28 days
Replace concept ID 28253:	With New PI:
Prescribing Instructions: State each of the 4 Eczema Area and Severity Index (EASI) symptom sub-score ratings (0 = none, 1 = mild, 2 = moderate, 3 = severe) for: (i) erythema, (ii) oedema/papulation, (iii) excoriation, (iv) lichenification Acceptable scores can be: (a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication. State the percentage face/hand surface area affected by the condition (must be at least 30%) where EASI symptom sub-scores are not provided. This percentage surface area can also be stated in addition to the EASI symptom sub-scores. The EASI/percentage surface area and DLQI baseline measurements are to form the basis of determining if an adequate response to treatment has been achieved under the Continuing treatment restriction. In addition to stating them in this authority application, document them in the patient's medical records. Document the details of the medium to high potency topical corticosteroids (or calcineurin inhibitors) initially trialled are in the patient's medical records.	**Prescribing Instructions:** State each of the 4 Eczema Area and Severity Index (EASI) symptom sub-score ratings (0 = none, 1 = mild, 2 = moderate, 3 = severe) for: (i) erythema, (ii) oedema/papulation, (iii) excoriation, (iv) lichenification Acceptable scores can be: (a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication. State the percentage face/hand surface area affected by the condition (must be at least 30%) where EASI symptom sub-scores are not provided. This percentage surface area can also be stated in addition to the EASI symptom sub-scores. The EASI/percentage surface area and DLQI baseline measurements are to form the basis of determining if an adequate response to treatment has been achieved under the Continuing treatment restriction. In addition to stating them in this authority application, document them in the patient's medical records. Document the details of the medium to high potency topical corticosteroids (or / calcineurin inhibitors/*JAK inhibitors*) initially trialled are in the patient's medical records.

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.