5.09 NEMOLIZUMAB, Powder for injection containing nemolizumab 30 mg with diluent in pre-filled dual-chamber pen, Nemluvio®, Galderma Australia Pty Ltd

1 Purpose of submission

1.1 This Category 2 submission requested a General Schedule Authority Required (Telephone/Online) listing of nemolizumab (NEMO) for the treatment of patients with severe atopic dermatitis affecting the whole body, face, and/or hands.

1.2 Listing was requested on the basis of a cost-minimisation approach (CMA) versus dupilumab (DUPI).

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Patients aged 12 years or older with chronic severe AD affecting the whole body or the face and/or hands, who are inadequately controlled on topical therapies.
Intervention	Nemolizumab (NEMO) 60 mg SC as an initial dose, followed by 30 mg SC given Q4W. After 16 weeks of treatment, NEMO 30 mg SC Q8W.
Comparator	In adult patients and in adolescents ≥ 60 kg: Dupilumab (DUPI) 600 mg SC injection as a loading dose followed by 300 mg SC injection Q2W In adolescents 30 kg to < 60 kg: DUPI 400 mg SC injection as a loading dose, followed by 200 mg SC injection Q2W
Outcomes	Primary outcomes: Proportion of patients with a 75% improvement in EASI score (EASI-75) at Week 16; proportion of patients achieving IGA score of 0 or 1 with a ≥ 2-point improvement at Week 16. Secondary outcomes: Proportion of patients achieving a 50% improvement in EASI score (EASI- 50); proportion of patients achieving a ≥ 4-point improvement in DLQI at Week 16; PP-NRS at Week 16. Post-hoc outcome: PBS response criteria: composite measure of response EASI-50 and improvement in DLQI ≥4-points, at Week 16. Safety outcomes: Proportion of patients experiencing AEs, SAEs and discontinuation of treatment due to AEs.
Clinical claim	For the treatment of patients aged 12 years or older with chronic severe AD affecting the whole body or the face and/or hands, who are inadequately controlled on topical therapies, NEMO is non-inferior to DUPI in terms of efficacy and safety, based on their recommended dosing schedules. In addition, NEMO offers the benefits of fewer injections and reduced rate of conjunctivitis, compared to DUPI.

Source: Table 1-1, p36 of the submission

AD = atopic dermatitis; AEs = adverse events; DLQI = Dermatology Life Quality Index; EASI = Eczema Area and Severity Index; IGA = Investigator's Global Assessment; PP-NRS = Peak Pruritus Numerical Rating Score; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous; PBS = Pharmaceutical Benefits Scheme; SAEs = serious adverse events

Note: IGA is equivalent to Physician's Global Assessment (PGA) in the commentary

2 Background

Registration status

2.1 TGA status at time of PBAC consideration: registered. The submission was made under the TGA/PBAC Parallel Process, with registration finalised on 27 May 2025. The approved TGA indication for NEMO is "for the treatment of moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or topical calcineurin inhibitors in adults and in patients aged 12 years and above who weigh at least 30 kg, who are candidates for systemic therapy".

3 Requested listing

Suggested additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough. For brevity reasons, an abridged restriction is presented in this section. A grandfather listing was proposed, but is not included below, also for brevity reasons. Refer to

3.1 Appendix A: Proposed Restrictions for the full proposed restriction.

Initial

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
NEMOLIZUMAB					
~~nemolizumab 30 mg/0.49 mL injection, 1 x 0.49 mL pen device~~ *Nemolizumab 30 mg injection [1 chamber] (&) inert substance diluent [1 chamber], 1 dual chamber pen device*	NEW	2	2	2	Nemluvio

Concept ID	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (telephone/electronic)
	Prescribing rule level:
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Initial treatment of the whole body
	Clinical criteria:
	Patient must have a Physicians Global Assessment (PGA) (5-point scale) baseline score of at least 4 as evidence of severe disease despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days
	AND
	Clinical criteria:
	Patient must have an Eczema Area and Severity Index (EASI) baseline score of at least 20 despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days
	AND
	Clinical criteria:
	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
	AND
	Clinical criteria:
	The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands
	AND
	Clinical criteria:
	Patient must not have experienced an inadequate response to this biological medicine in this PBS indication
	AND
	~~**Treatment**~~ ***Clinical*** **criteria:**
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Initial treatment of the face and/or hands
	Clinical criteria:

	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 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
	AND
	Clinical criteria:
	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
	AND
	Clinical criteria:
	The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	AND
	Clinical criteria:
	Patient must not have experienced an inadequate response to this biological medicine in this PBS indication

Continuing

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
NEMOLIZUMAB					
~~nemolizumab 30 mg/0.49 mL injection, 1 x 0.49 mL pen device~~ *Nemolizumab 30 mg injection [1 chamber] (&) inert substance diluent [1 chamber], 1 dual chamber pen device*	NEW	1	1	2	Nemluvio

Concept ID	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (telephone/electronic)
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Continuing or resuming treatment of the whole body
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the whole body
	AND
	Clinical criteria:
	~~Patient must have achieved an adequate response prior to this first continuing treatment authority application; or~~ *Patient must have achieved an adequate response within the first 16 weeks of treatment; or*
	Patient must have maintained an adequate response to their most recent course of PBS-subsidised treatment with this biological medicine for this PBS indication if this is the second or subsequent Continuing treatment authority application; or

	Patient must have temporarily ceased treatment for reasons other than lack of response (e.g. family planning, vaccination with live vaccines, adverse-effect investigation), thereby being unable to achieve/maintain an adequate response immediately prior to this authority application
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Continuing or resuming treatment of the face and/or hands
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the face/hands
	AND
	Clinical criteria:
	~~Patient must have achieved an adequate response prior to this first continuing treatment authority application; or~~ *Patient must have achieved an adequate response within the first 16 weeks of treatment; or*
	Patient must have maintained an adequate response to their most recent course of PBS-subsidised treatment with this biological medicine for this PBS indication if this is the second or subsequent Continuing treatment authority application; or
	Patient must have temporarily ceased treatment for reasons other than lack of response (e.g. family planning, vaccination with live vaccines, adverse-effect investigation), thereby being unable to achieve/maintain an adequate response immediately prior to this authority application
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication

3.2 A Special Pricing Arrangement (SPA) was requested for NEMO as for other systemic treatments for severe AD, including DUPI and upadacitinib (UPA). The submission noted that the effective approved ex-manufacturer price (AEMP) of DUPI remains confidential and thus, the sponsor was unable to accurately nominate an effective ex-manufacturer price (EMP) for NEMO.

3.3 The submission requested the listing of the pre-filled 30 mg pen which is administered by subcutaneous (SC) injection. The recommended dosage is an initial dose of 60 mg, followed by 30 mg every 4 weeks (Q4W) for 16 weeks, and then 30 mg every 8 weeks (Q8W). The proposed maximum quantities and number of repeats of NEMO provide sufficient supply for the loading dose and treatment up to Week 16 under the initial treatment phase and for 6 months under the continuing treatment phase.

3.4 The requested PBS indication for NEMO treatment is narrower than the proposed TGA indication (i.e. it is for severe AD whereas the TGA indication is for moderate to severe AD). The requested restrictions for initial and continuing treatment of NEMO align with the current PBS listings for DUPI and UPA.

3.5 The requested PBS restrictions for NEMO generally reflect the NEMO trial populations, except that the clinical trials included both patients with severe AD and those with

moderate AD. The submission presented post hoc subgroup analyses in severe AD patients from the NEMO trials.

3.6 The Eczema Area and Severity Index (EASI), Dermatology Life Quality Index (DLQI), and Physician's Global Assessment (PGA) are assessment tools that assist clinicians to identify patients with severe disease who are eligible for treatments and are referenced in the clinical criteria in the proposed PBS restriction for NEMO and in the current PBS listing for DUPI. To be eligible to initiate NEMO and DUPI, patients must have severe AD, defined as an EASI baseline score of ≥ 20 and a PGA (5-point scale) baseline score of ≥ 4.

3.7 The Pre-Sub-Committee Response (PSCR) proposed to include an extended induction restriction to allow patients an additional 8 weeks of Q4W treatment for patients who have not responded at Week 16. The ESC noted PBAC's advice from March 2024 for lebrikizumab relating to an extended induction restriction: "The PBAC noted that this approach is not consistent with induction and assessment of response for DUPI and UPA, but noted that it was consistent with the clinical data presented for LEB. The PBAC also noted that, in general, clinical practice with biologicals is moving towards a more extended induction period for assessment of response. The PBAC noted that there was potentially a higher cost associated with this approach as patients without adequate response are treated for a longer period before discontinuing treatment and slower responders receive additional doses compared with patients who respond by Week 16. The PBAC considered that inclusion of the extended induction period with assessment at 24 weeks, as proposed for the LEB restrictions, was reasonable, but the additional doses would need to be accounted for in the calculation of equi-effective doses applied in the cost-minimisation approach." (paragraph 3.3, lebrikizumab Public Summary Document (PSD), March 2024 PBAC meeting).

3.8 The ESC considered that an extended induction period for NEMO was not appropriate as the requested dosing regimen of an additional 8 weeks of Q4W dosing was not included in the approved TGA Product Information (PI), unlike the lebrikizumab PI which explicitly describes the extended induction regimen. The Pre-PBAC response (noted that the EMA PI for NEMO states "Some patients with initial partial response may further improve with continued treatment beyond 16 weeks", noting that it is not uncommon for delays in harmonisation of the PI. The PBAC noted a similar statement appears in the draft Australian PI only for the prurigo nodularis indication, but not for the atopic dermatitis indication.

3.9 The submission also proposed grandfather restrictions for approximately 200 patients that are anticipated to be enrolled in a Patient Familiarisation Program prior to PBS listing.

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

4 Population and disease

4.1 AD is the most common chronic inflammatory skin disease that affects 15% to 20% of children and up to 10% of adults[1]. Approximately 60% of patients develop AD in the first year of life and 90% within the first 5 years of life[2]. The condition is associated with other atopic manifestations such as asthma, allergic rhinitis, or food allergy[3]. AD is presented as areas of rashes and dryness with intense pruritus that commonly involve the creases of the elbows, behind the knees, across the ankles and may also involve the face, ears, and neck. The condition is often relapsing and affected patients are predisposed to bacterial and viral skin infections. AD involving the eyelid can cause blepharitis (general inflammation and redness of the eyelid) and conjunctivitis. AD impacts an individual's overall quality of life (QoL), as well as social, academic, and occupational performance, and 33% to 90% of affected adults have AD associated sleep disturbance[4,5].

4.2 AD is caused by a complex interaction between genetics, skin barrier dysfunction, immune dysregulation, and extrinsic factors resulting in cutaneous inflammation and related symptoms. The Janus kinase (JAK)-signal transducer and activator of transcription pathway results in the release of cytokines including interleukin (IL)-4, IL-13 and IL-31 that are responsible for the pathogenesis of AD and the cardinal symptoms of AD, such as pruritus[6].

4.3 Based on the current Australian and international management guidelines for AD[7,8], a stepwise approach is applied. The baseline management includes optimal skin care with emollients/moisturisers, bathing practice, adjuvant therapy, and specific skin therapy during acute flares. Patients with severe AD who cannot achieve adequate disease control[9] despite on topical corticosteroid (TCS) or topical calcineurin inhibitor (TCI) for ≥ 28 days are eligible for systemic treatment with immunosuppressants, monoclonal antibody, and JAK inhibitor as options.

---

[1] Allergy & Anaphylaxis Australia. Eczema (atopic dermatitis). URL: https://allergyfacts.org.au/__interest/eczema/

[2] Eichenfield LF et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. Journal of the American Academy of Dermatology. 2014; 70(2): 338-351.

[3] Berke R, Singh A & Guralnick M. Atopic dermatitis: an overview. American Family Physician. 2012; 86(1): 35-42.

[4] Drucker AM et al. The Burden of Atopic Dermatitis: Summary of a Report for the National Eczema Association. Journal of Investigative Dermatology. 2017; 137(1): 26-30.

[5] Bawany F et al. Sleep Disturbances and Atopic Dermatitis: Relationships, Methods for Assessment, and Therapies. The Journal of Allergy and Clinical Immunology: In Practice. 2021; 9(4): 1488-1500.

[6] Dubin C, Del Duca E & Guttman-Yassky E. The IL-4, IL-13 and IL-31 pathways in atopic dermatitis. Expert Review of Clinical Immunology. 2021; 17(8): 835-852.

[7] Smith S et al. Atopic dermatitis in adults: An Australian management consensus. Australasian Journal of Dermatology. 2020; 61(1): 23-32.

[8] Wollenberg A et al. European guideline (EuroGuiDerm) on atopic eczema: part I - systemic therapy. Journal of the European Academy of Dermatology and Venereology. 2022; 36(9): 1409-1431.

[9] Refers to a state in which symptoms are absent or mild without daily activities being disturbed by AD (Smith et al. 2020)

4.4 NEMO is a first in class humanised monoclonal antibody (IgG2) that inhibits interleukin-31 (IL-31). IL-31 is one of the key cytokines responsible for pruritus and inflammation in AD. In the NEMO product information (PI), it is stated that NEMO can be used with TCSs and TCIs. Any use of topical therapies should be tapered and subsequently discontinued when the disease has sufficiently improved.

4.5 NEMO, if listed on the PBS, provides an additional option of systemic treatment for severe AD in patients who are inadequately controlled on topical therapies. The Advisory Committee on Medicine, an expert advisory committee of the TGA, considered that NEMO could be an option for those patients who have failed other systemic therapies, before moving on to other alternative therapies with less favourable side effect profile, such as JAK inhibitors. The ACM acknowledged that NEMO could potentially provide an alternative option for patients who don't respond completely to DUPI or for those who cannot tolerate its adverse effects, although the registered indication does not restrict use to after DUPI use.

5 Comparator

5.1 DUPI was the nominated main comparator in the submission.

5.2 The main arguments provided in the submission to support the nomination of DUPI as the main comparator included: 1) DUPI is the most utilised targeted therapy for treating severe AD in clinical practice (approximately 87% of PBS services) and hence is the therapy most likely to be replaced by NEMO should NEMO be listed, and 2) in the submissions for other targeted therapies for severe AD (UPA, lebrikizumab [LEB], and abrocitinib [ABRO]), DUPI was accepted as the main comparator on a cost-minimisation basis.

5.3 The ESC considered that DUPI was the appropriate main comparator.

5.4 UPA (a JAK1 inhibitor) is an alternate PBS-listed targeted therapy for severe AD. However, UPA is less frequently used than DUPI in clinical practice. LEB and ABRO have been recommended by the PBAC at the March 2024 PBAC meeting and the November 2024 PBAC meeting, respectively, but were not PBS listed at time of PBAC consideration

5.5 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the *National Health Act 1953*, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.

5.6 For the requested population, the following PBS-listed medicines may be considered alternative therapies because they could be replaced in practice: DUPI and UPA.

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

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician noted that there is a need for nemolizumab as an alternative agent for atopic dermatitis because there are patients who are not responding to available agents, or who cannot use the available agents because of pregnancy or history of thromboembolic disease, major adverse cardiac events, leukaemias and other malignancies. The clinician described some of the advantages of NEMO over DUPI including it can be kept out of fridge for longer, may have better patient adherence and improved management of conjunctivitis.

6.2 The clinician noted that although there is limited data directly comparing DUPI and NEMO, the evidence demonstrates that NEMO has the same outcomes at Week 24 when given an extra dose at Week 20, compared to DUPI at Week 16. Furthermore, the clinician stated it is plausible and reasonable for the inclusion of an extended induction period from Week 16 for NEMO to allow a group of patients who are at risk of not responding to treatment to demonstrate a response at 24 weeks.

Consumer comments

6.3 The PBAC noted and welcomed the input from health care professionals (1) and organisations (3) via the Consumer Comments facility on the PBS website. The PBAC noted inputs received from the Australasian College of Dermatologists (ACD), Eczema Support Australia and a joint submission between Allergy & Anaphylaxis Australia, Australasian Society of Clinical Immunology and Allergy (ASCIA) and the National Allergy Council, which were all in support of listing nemolizumab on the PBS.

6.4 All inputs stated that atopic dermatitis can impact an individual's ability to participate in social, work, and educational activities. Itch is often cited as a major debilitating component of atopic dermatitis, resulting in broken painful skin and an increased risk of infection often results in social isolation with poor sleep and low self-esteem contributing to a poor quality of life. The inputs also noted the mental health struggle associated with their condition, including anxiety, self-image issues, and the sheer exhaustion and hopelessness it can bring. The emotional distress also extends to families. One of the inputs noted there is a persistent frustration with the misconception that eczema is "just a rash" and that people "just grow out of it" when in reality, it is a persistent, lifelong, and debilitating condition that affects individuals in vastly different ways.

6.5 The inputs all noted the improvement to patient lives through the current therapies like biologics and JAK Inhibitors. Input also noted the risks to patient outcomes if supply or access issues emerge where there is only one biologic agent available for patients and argued there is a need for alternative treatments for atopic dermatitis for patients who do not get a good or complete response to currently available treatments. The inputs noted NEMO has a different mechanism of action and safety profile compared to other treatments currently available. The inputs noted NEMO

may assist with improved management and therefore, improve quality of life, for some people with severe atopic dermatitis, particularly those who have tried other treatments.

6.6 Eczema Support Australia noted that even where trials show similar outcomes, differences in tolerability, symptom relief (especially itch), and safety profiles—such as with nemolizumab, can be significant to patients. These lived experiences and values are not always captured in clinical metrics but are vital to real-world care.

Clinical trials

6.7 No head-to-head trials comparing NEMO and DUPI were available. Instead, indirect treatment comparisons (ITCs), using the Bucher methodology via placebo as the common reference group, were used to support the submission's claim of non-inferior efficacy and safety. The trials included in the ITCs were:

- Four NEMO trials: ARCADIA 1 (N = 941), ARCADIA 2 (N = 787), ARCADIA CYLO (N = 276), and Study 114322 (N = 114).
- Three DUPI trials: CAFÉ (N = 215), CHRONOS (N = 421), and JADE COMPARE (N = 373). These trials have previously been seen by the PBAC in the DUPI, UPA, LEB and ABRO submissions.

6.8 The included NEMO and DUPI trials all enrolled patients with moderate to severe AD, which is broader than the proposed PBS population of severe AD only and defined as an EASI score ≥ 20 and an PGA/Investigator's Global Assessment (IGA) score of 4. Subgroup analyses of patients with severe AD of the NEMO trials were presented. But corresponding severe AD subgroup analyses in the included DUPI trials were not performed due to the lack of data. Therefore, comparative evidence of NEMO versus DUPI in severe AD patients was not presented.

6.9 ARCADIA CYLCO and CAFÉ were included in the ITCs for safety but not in the ITCs for efficacy, as these trials enrolled patients who had previously been treated with systemic cyclosporine A (CsA). This appeared reasonable as, in Australian clinical practice, the use of systemic immunosuppressive therapies is only prescribed to patients who have exhausted biological options and data from the 10% PBS sample indicate that their use is low in the target population.

6.10 As all NEMO trials included background therapy with TCSs and/or TCIs, the DUPI trials used to inform the ITCs were restricted to those in which concomitant therapy with TCS was allowed. This was appropriate and reduced the transitivity concerns to some extent. The inclusion of DUPI trials without background therapy with TCSs (such as SOLO 1 and SOLO 2) would have biased the ITC results in favour of DUPI.

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
Nemolizumab		
ARCADIA 1 NCT03985943 **ARCADIA 2** NCT03989349	ARCADIA 1 CSR (NCT03985943) Efficacy and safety of nemolizumab in subjects with moderate-to-severe atopic dermatitis ARCADIA 2 CSR (NCT03989349) Efficacy & safety of nemolizumab in subjects with moderate-to-severe atopic dermatitis Silverberg, J. I., Wollenberg, A., et al. Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2): results from two replicate, double-blind, randomised controlled phase 3 trials.	18 September 2023 19 September 2023 *The Lancet* 2024; 404(10451) 445-460
ARCADIA CYCLO NCT05056779 EUCTR2021-002166-40	ARCADIA CYCLO CSR Efficacy and safety of nemolizumab in subjects with moderate-to-severe atopic dermatitis with inadequate response to or for whom cyclosporine A is not medically advisable	21 February 2024
Study 114322 NCT03100344 EUCTR2016-005025-37	Study 114322 CSR Dose-ranging study of nemolizumab in atopic dermatitis Silverberg, J. I., Pinter, A., et al. Phase 2B randomized study of nemolizumab in adults with moderate-to-severe atopic dermatitis and severe pruritus	29 May 2019 *Journal of Allergy & Clinical Immunology* 2020; 145(1)173-182
Dupilumab		
LIBERTY AD CAFÉ NCT02755649	A study to assess the efficacy and safety of dupilumab in participants with severe atopic dermatitis (AD) that are not controlled with oral cyclosporine A (CSA) or for those who cannot take oral CSA because it is not medically advisable. https://clinicaltrials.gov/study/NCT02755649 de Bruin-Weller, M., Thaci, D., et al. Dupilumab with concomitant topical corticosteroid treatment in adults with atopic dermatitis with an inadequate response or intolerance to ciclosporin A or when this treatment is medically inadvisable: a placebo-controlled, randomized phase III clinical trial (LIBERTY AD CAFÉ)	August 2020 *British Journal of Dermatology* 2018; 178(5) 1083-1101
LIBERTY AD CHRONOS NCT02260986	Study to assess the efficacy and long-term safety of dupilumab (REGN668/SAR231893) in adult participants with moderate-to-severe atopic dermatitis (CHRONOS). https://clinicaltrials.gov/study/NCT02260986 Blauvelt, A., de Bruin-Weller, M., et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial	October 2017 *The Lancet* 2017; 389(10086) 2287-2303
JADE COMPARE NCT03720470	Study evaluating efficacy and safety of PF-04965842 and dupilumab in adult subjects with moderate to severe stopic dermatitis on background topical therapy (JADE Compare). https://clinicaltrials.gov/study/NCT03720470 Bieber, T., Simpson, E. L., et al. Abrocitinib versus placebo or dupilumab for atopic dermatitis	January 2021 *New England Journal of Medicine* 2021; 384(12) 1101-1112

Source: Table 2-5, p78-83 of the submission.
CSR = clinical study report.
Notes: Including key study publications only.
Blue shading indicates studies previously seen by the PBAC.

6.12 The key features of the included evidence are summarised in Table 3.

Table 3: Key features of the included evidence – indirect comparison

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes	Used in CMA
Nemolizumab vs. placebo						
ARCADIA 1	941	R, DB, MC 48 weeks	Low	Adult and adolescent patients with moderate to severe AD with inadequate response to topical steroids	EASI-75 IGA success EASI-50 ≥4-point improvement in DLQI ≥4-point improvement in PP-NRS Safety	Used
ARCADIA 2	787	R, DB, MC 48 weeks	Low	Adult and adolescent patients with moderate to severe AD with inadequate response to topical steroids	EASI-75 IGA success EASI-50 ≥4-point improvement in DLQI ≥4-point improvement in PP-NRS Safety	Used
ARCADIA CYCLO	276	R, DB, MC 16 weeks	Low	Adult patients with moderate to severe AD with recent exposure to CsA or medically inadvisable to received CsA	EASI-75 IGA success EASI-50 Safety	Not used
Study 114322	114	R, DB, MC 24 weeks	Low	Adult patients with moderate to severe AD with inadequate response to topical steroids	EASI-75 IGA success EASI-50 ≥4-point improvement in DLQI Safety	Used
Meta-analysis	2118	Included ARCADIA 1, ARCADIA 2, and Study 114322 for efficacy and ARCADIA 1, ARCADIA 2, ARCADIA CYCLO, and Study 114322 for safety.				Not used
Dupilumab vs placebo						
CHRONOS	421	R, DB, MC 1 year	Low	Adult patients with moderate to severe AD with inadequate response to topical steroids	EASI-75 IGA success EASI-50 ≥4-point improvement in DLQI ≥4-point improvement in PP-NRS Safety	Used
JADE COMPARE	373	R, DB, MC 24 weeks.	Low	Adult patients with moderate to severe AD with inadequate response to topical steroids	EASI-75 IGA success EASI-50 ≥4-point improvement in DLQI ≥4-point improvement in PP-NRS Safety	Used
CAFÉ	215	R, DB, MC 16 weeks	Low	Adult patients with moderate to severe AD with inadequate response to topical steroids	EASI-75 IGA success EASI-50 ≥4-point improvement in DLQI ≥4-point improvement in PP-NRS Safety	Not used
Meta-analysis	1009	Included CHRONOS, and JADE COMPARE for efficacy and CHRONOS, JADE COMPARE, and CAFÉ for safety.				Not used

Source: Compiled during the evaluation, based on Section 2.3.2, pp86-91 and Table 2-26, 146 of the submission.
AD = atopic dermatitis; CMA =cost minimisation approach; CsA = cyclosporine A; DB = double blind; DLQI = Dermatology Life Quality Index; EASI-50/75 = improvement of at least 50%/75% from baseline in Eczema Area and Severity Index; IGA = Investigator's Global Assessment; MC = multi-centre; PP-NRS = Peak Pruritus Numerical Rating Score; R = randomised.
Note: some trials had multiple intervention treatment arms, only those which used the recommended dose regimens for NEMO and DUPI were presented in the submission.
Blue shading indicates data previously seen by the PBAC.

6.13 All of the NEMO and DUPI trials were randomised, double-blind, placebo-controlled trials and were at a low risk of bias within individual studies. However, the ITCs were at a higher risk of bias due to transitivity concerns between the NEMO and DUPI trials:

- Two of the NEMO trials with the largest sample size, i.e. ARCADIA 1 and ARCADIA 2, enrolled patients aged ≥12 years; whereas all included DUPI trials and the other two NEMO trials included adult patients ≥18 years of age only.
- Of the trials included in the efficacy ITCs, ARCADIA 1, ARCADIA 2, CHRONOS and JADE COMPARE required patients to have an EASI score of ≥16 at baseline, compared to an EASI score of ≥12 in Study 114322.
- The proportion of patients having an IGA of 4 (corresponds to severe AD) at baseline was lower in NEMO trials than in DUPI trials (31% vs. 40%).

The direction and magnitude of the impact of the observed differences across trial sets on the ITC results could not be accurately estimated; however, the ESC noted that the placebo response rates across the NEMO and DUPI trials were similar.

6.14 The submission provided data on the baseline patient characteristics in the severe AD subgroup (as defined in the PBS restriction) of the NEMO trials. Overall, the NEMO and placebo treatment arms in the subgroup were comparable in terms of the demographics and disease characteristics presented in the submission despite it not being a prespecified subgroup.

6.15 The primary endpoints in the submission were EASI-75, which corresponds to a ≥ 75% improvement in EASI from baseline, and IGA success, defined as achieving an IGA score of 0 (clear) or 1 (almost clear) and a ≥2-point improvement in IGA score from baseline. EASI-50 was one of the key secondary outcomes. The other secondary outcome, ≥4-point improvement in DLQI outcome, was calculated post hoc based on individual patient data from the NEMO trials. This allowed for the submission to report the PBAC preferred composite outcome of EASI-50 and ≥4-point improvement in DLQI for assessment of treatments for severe AD.

Comparative effectiveness

<u>ITCs of NEMO versus DUPI in the intention-to-treat (ITT) population of patient with moderate and severe AD</u>

6.16 Table 4 toTable 7 summarise the results of primary endpoints (EASI-75 and IGA success) and key secondary outcomes (EASI-50 and ≥4-point improvement in DLQI) specified in the submission at Week 16 in the NEMO and DUPI trials, as well as the ITC results. ITCs for the PBAC preferred composite endpoint of EASI-50 and ≥4-point improvement in DLQI were not performed, due to the lack of data in the comparator DUPI trials.

Table 4: ITC of NEMO 30 mg Q4W vs DUPI 300 mg Q2W: EASI-75 at Week 16 (NRI) – ITT population

	Intervention n/N (%)	Comparator n/N (%)	RR (95% CI)	RD (95% CI)
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	270/620 (43.5)	93/321 (29.0)	**1.50 (1.24,1.82)**	**0.15 (0.08, 0.21)**
ARCADIA 2	220/522 (42.1)	80/265 (30.2)	**1.40 (1.13, 1.72)**	**0.12 (0.05, 0.19)**
Study 114322	28/57 (49.1)	11/57 (19.3)	**2.55 (1.41, 4.61)**	**0.30 (0.13, 0.46)**
ARCADIA CYCLO	65/138 (47.1)	48/138 (34.8)	**1.35 (1.01, 1.81)**	**0.12 (0.01, 0.24)**
Pooled (REM)			**1.48 (1.27, 1.72)**	**0.15 (0.10, 0.20)**
Pooled (REM) excl. ARCADIA CYCLO			**1.54 (1.25, 1.89)**	**0.16 (0.09, 0.22)**
DUPI 300 mg Q2W vs placebo				
CHRONOS	73/106 (68.9)	73/315 (23.2)	**2.97 (2.34, 3.77)**	**0.46 (0.36, 0.56)**
JADE COMPARE	152/232 (65.5)	38/124 (30.6)	**2.14 (1.62, 2.83)**	**0.35 (0.25, 0.45)**
CAFÉ	67/107 (62.6)	32/108 (29.6)	**2.11 (1.53, 2.93)**	**0.33 (0.20, 0.46)**
Pooled (REM)			**2.42 (1.90, 3.07)**	**0.38 (0.30, 0.46)**
Pooled (REM) excl. CAFÉ			**2.54 (1.83, 3.54)**	**0.40 (0.30, 0.51)**
Indirect comparison				
NEMO 30 mg Q4W (pooled excl. ARCADIA CYCLO) vs DUPI 300 mg Q2W (pooled excl. CAFÉ)			**0.61 (0.41, 0.90)**	**-0.24 (-0.37, -0.12)**

Source: Table 2-83, p213 of the submission.
CI = confidence interval; DUPI = dupilumab; EASI-75 = proportion of patients with ≥ 75% improvement in Eczema Area and Severity Index from baseline; ITC = indirect treatment comparison; ITT = intention-to-treat; NEMO = nemolizumab; NRI = non responder imputation; Q2W = every 2 weeks; Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk
Bold = statistically significant
Blue shading indicates data previously seen by the PBAC.

Table 5: ITC of NEMO 30 mg Q4W vs DUPI 300 mg Q2W: IGA success at Week 16 (NRI) – ITT population

	Intervention n/N (%)	Comparator n/N (%)	RR (95% CI)	RD (95% CI)
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	221/620 (35.6)	79/321 (24.6)	**1.45 (1.16, 1.80)**	**0.11 (0.05, 0.17)**
ARCADIA 2	197/522 (37.7)	69/265 (26.0)	**1.45 (1.15, 1.83)**	**0.12 (0.05, 0.18)**
Study 114322	19/57 (33.3)	7/57 (12.3)	**2.71 (1.24, 5.95)**	**0.21 (0.06, 0.36)**
ARCADIA CYCLO	25/138 (18.1)	20/138 (14.5)	1.25 (0.73, 2.14)	0.04 (-0.05, 0.12)
Pooled (REM)			**1.47 (1.26, 1.70)**	**0.11 (0.06, 0.16)**
Pooled (REM) excl. ARCADIA CYCLO			**1.50 (1.25, 1.79)**	**0.12 (0.18, 0.16)**
DUPI 300 mg Q2W vs placebo				
CHRONOS	41/106 (38.7)	39/315 (12.3)	**3.12 (2.14, 4.56)**	**0.26 (0.16, 0.36)**
JADE COMPARE	90/232 (38.8)	16/124 (12.9)	**3.01 (1.85, 4.88)**	**0.26 (0.17, 0.35)**
CAFÉ	43/107 (40.2)	15/108 (13.9)	**2.89 (1.71, 4.88)**	**0.26 (0.15, 0.38)**
Pooled (REM)			**3.03 (2.34, 3.90)**	**0.26 (0.20, 0.32)**
Pooled (REM) excl. CAFÉ			**3.08 (2.28, 4.15)**	**0.26 (0.20, 0.33)**
Indirect comparison				
NEMO 30 mg Q4W (pooled excl. ARCADIA CYCLO) vs DUPI 300 mg Q2W (pooled excl. CAFÉ)			**0.49 (0.34, 0.69)**	**-0.14 (-0.22, -0.06)**

Source: Table 2-84, p213 of the submission.
CI = confidence interval; DUPI = dupilumab; IGA = Investigator's Global Assessment; ITC = indirect treatment comparison; ITT = intention-to-treat; NEMO = nemolizumab; NRI = non responder imputation; Q2W = every 2 weeks; Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk
Bold = statistically significant
Blue shading indicates data previously seen by the PBAC.

Table 6: ITC of NEMO 30 mg Q4W vs DUPI 300 mg Q2W: EASI-50 at Week 16 (NRI) – ITT population

	Intervention n/N (%)	Comparator n/N (%)	RR (95% CI)	RD (95% CI)
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	371/620 (59.8)	155/321 (48.3)	**1.24 (1.09, 1.41)**	**0.12 (0.05, 0.18)**
ARCADIA 2	323/522 (61.9)	130/265 (49.1)	**1.26 (1.10, 1.45)**	**0.13 (0.06, 0.20)**
Study 114322	34/57 (59.6)	21/57 (36.8)	**1.70 (1.13, 2.57)**	**0.25 (0.07, 0.42)**
ARCADIA CYCLO	60/138 (43.5)	46/138 (33.3)	1.30 (0.96, 1.77)	0.10 (-0.01, 0.22)
Pooled (REM)			**1.27 (1.16, 1.39)**	**0.13 (0.08, 0.17)**
Pooled (REM) excl. ARCADIA CYCLO			**1.27 (1.15, 1.40)**	**0.13 (0.08, 0.18)**
DUPI 300 mg Q2W vs placebo				
CHRONOS	85/106 (80.2)	118/315 (37.5)	**2.14 (1.80, 2.54)**	**0.43 (0.33, 0.52)**
JADE COMPARE	195/232 (84.1)	71/124 (57.3)	**1.47 (1.25, 1.73)**	**0.27 (0.17, 0.37)**
CAFÉ	91/107 (85.0)	47/108 (43.5)	**1.95 (1.55, 2.46)**	**0.42 (0.30, 0.53)**
Pooled (REM)			**1.82 (1.43, 2.33)**	**0.37 (0.27, 0.47)**
Pooled (REM) excl. CAFÉ			**1.77 (1.22, 2.57)**	**0.35 (0.19, 0.51)**
Indirect comparison				
NEMO 30 mg Q4W (pooled excl. ARCADIA CYCLO) vs DUPI 300 mg Q2W (pooled excl. CAFÉ)			0.72 (0.49, 1.05)	**-0.22 (-0.39, -0.05)**

Source: Table 2-85, p214 of the submission.
CI = confidence interval; DUPI = dupilumab; EASI-50 = proportion of patients with ≥ 50% improvement in Eczema Area and Severity Index from baseline; ITC = indirect treatment comparison; ITT = intention-to-treat; NEMO = nemolizumab; NRI = non responder imputation; Q2W = every 2 weeks; Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk
Bold = statistically significant
Blue shading indicates data previously seen by the PBAC.

Table 7: ITC of NEMO 30 mg Q4W vs DUPI 300 mg Q2W: ≥4-point improvement in DLQI at Week 16 (NRI)

	Intervention n/N (%)	Comparator n/N (%)	RR (95% CI)	RD (95% CI)
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	379/535 (70.8)	160/272 (58.8)	**1.20 (1.08, 1.35)**	**0.12 (0.05, 0.19)**
ARCADIA 2	300/431 (69.6)	118/224 (52.7)	**1.32 (1.15, 1.52)**	**0.17 (0.09, 0.25)**
Study 114322	31/47 (66.0)	28/42 (66.6)	0.99 (0.74, 1.33)	-0.01 (-0.20, 0.19)
ARCADIA CYCLO	NA	NA	NA	NA
Pooled (REM)			**1.25 (1.14, 1.37)**	**0.14 (0.09, 0.19)**
Pooled (REM) excl. ARCADIA CYCLO			**1.25 (1.14, 1.37)**	**0.14 (0.09, 0.19)**
DUPI 300 mg Q2W vs placebo				
CHRONOS	81/100 (81.0)	129/300 (43.0)	**1.88 (1.60, 2.21)**	**0.38 (0.29, 0.47)**
JADE COMPARE	191/229 (83.4)	71/119 (59.7)	**1.40 (1.19, 1.64)**	**0.24 (0.14, 0.34)**
CAFÉ	85/97 (87.6)	42/95 (44.2)	**1.98 (1.56, 2.52)**	**0.43 (0.32, 0.55)**
Pooled (REM)			**1.72 (1.38, 2.15)**	**0.35 (0.23, 0.46)**
Pooled (REM) excl. CAFÉ			**1.62 (1.21, 2.18)**	**0.31 (0.17, 0.45)**
Indirect comparison				
NEMO 30 mg Q4W (pooled excl. ARCADIA CYCLO) vs DUPI 300 mg Q2W (pooled excl. CAFÉ)			0.77 (0.57, 1.05)	**-0.17 (-0.32, -0.02)**

Source: Table 2-86, p215 of the submission.
CI = confidence interval; DUPI = dupilumab; DLQI = Dermatology Life Quality Index; ITC = indirect treatment comparison; NA = not available; NEMO = nemolizumab; NRI = non responder imputation; Q2W = every 2 weeks; Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk
Bold = statistically significant
Blue shading indicates data previously seen by the PBAC.

6.17 NEMO was associated with an improvement in EASI-75, IGA success, EASI-50, and ≥4-point improvement in DLQI at Week 16, compared with placebo in most of the trials.

The differences were not statistically significant in Study 114322 for ≥4-point improvement in DLQI, and in ARCADIA CYCLO for the outcomes of IGA success and EASI-50 (data on ≥4-point improvement in DLQI was not reported in this study). The results of random effects meta-analyses showed that NEMO was statistically significantly superior to placebo for all four of the efficacy outcomes, regardless of whether ARCADIA CYCLO was included in the analyses or not.

6.18 The ESC noted the results of the ITCs suggested that NEMO had inferior efficacy in comparison to DUPI for the treatment of moderate and severe AD, for all efficacy outcomes, with differences reaching statistical significance for both primary endpoints of EASI-75 (relative risk [RR] = 0.61, 95% confidence interval [CI]: 0.41, 0.90; risk difference [RD] = -0.24, 95% CI: -0.37, -0.12) and IGA success (RR = 0.49, 95% CI: 0.34, 0.69; RD = -0.14, 95% CI: -0.22, -0.06) at Week 16. The results numerically favoured DUPI, but were not statistically significant, for the key secondary outcomes of EASI-50 (RR = 0.72, 95% CI: 0.49, 1.05; RD: -0.22, 95% CI: -0.39, -0.05) and ≥4-point improvement in DLQI (RR = 0.77, 95% CI: 0.57, 1.05; RD: -0.17, 95% CI: -0.32, -0.02).

6.19 Efficacy results of NEMO with a longer treatment duration were reported in the ARCADIA 1 and ARCADIA 2 trials. Table 8 presents the results of EASI-75, IGA success, and EASI-50 at Week 48 in ARCADIA 1 and ARCADIA 2. Data on DLQI improvement of ≥4 points at Week 48 were not reported in these trials.

6.20 The dosing regimen recommended in the PI is NEMO 30 mg Q4W for 16 weeks followed by NEMO 30 mg Q8W. Patients treated with NEMO 30 mg Q8W during the maintenance period reported numerically better results than patients in the placebo arm at Week 48, but the differences were modest in both trials (for example: RRs of 1.07 to 1.15 for EASI-75; RR = 1.05 for IGA success). No formal statistical analyses were prespecified for these data.

Table 8: Results of EASI-75, IGA success, and EASI-50 at Week 48 in ARCADIA 1 and ARCADIA 2 – enrolled patients in the MTP population

	ARCADIA 1				ARCADIA 2			
Treatment in ITP	**NEMO 30 mg Q4W**			**Placebo**	**NEMO 30 mg Q4W**			**Placebo**
Treatment in MTP	**NEMO 30 mg Q8W N = 91**	**NEMO 30 mg Q4W N = 90**	**Placebo N = 91**	**Placebo N = 100**	**NEMO 30 mg Q8W N = 78**	**NEMO 30 mg Q4W N = 79**	**Placebo N = 78**	**Placebo N = 85**
EASI-75, n (%)	67 (73.6)	67 (74.4)	55 (60.4)	64 (64.0)	61 (78.2)	62 (78.5)	53 (67.9)	62 (72.9)
IGA success, n (%)	48 (52.7)	54 (60.0)	38 (41.8)	50 (50.0)	54 (69.2)	50 (63.3)	46 (59.0)	56 (65.9)
EASI-50, n (%)	79 (86.8)	74 (82.2)	62 (68.1)	73 (73.0)	69 (88.5)	65 (82.3)	59 (75.6)	71 (83.5)

Source: Table 2-31, p155, Table 2-34, p158, and Table 2-36, p159 of the submission.
EASI-75/50 = proportion of patients with ≥ 50%/75% improvement in Eczema Area and Severity Index from baseline; IGA = Investigator's Global Assessment; ITP = initial treatment period; MTP = maintenance treatment period; NEMO = nemolizumab; Q4W = every 4 weeks; Q8W = every 8 weeks

6.21 The PSCR included additional analyses from the long-term extension (LTE) study of ARCADIA 1 and ARCADIA 2 to demonstrate the effects of an extended induction phase after an additional 8 and 20 weeks of NEMO Q4W in patients who did not respond to the initial induction period of NEMO Q4W for 16 weeks (see Table 9). The PSCR acknowledged the limitations of the naïve comparisons (i.e. not adjusted for placebo,

different denominators for the ARCADIA trials and the LTE, as well transitivity issues that bias the results against NEMO).

Table 9: Results of the LTE study: proportion of additional patients who respond with an additional 8 or 20 weeks of induction treatment with NEMO

Population	Outcome	LTE, N	LTE baseline response, n	N available to respond	Response at timepoint, n	Additional responders, n	% additional response from LTE*
8 weeks							
ITT	EASI-75	937	356	581	531	175	**30.1%**
ITT	IGA 0/1	937	273	664	337	64	**9.6%**
PBS**	EASI-50	172	59	113	98	39	**34.5%**
20 weeks							
ITT	EASI-75	937	356	581	569	213	**36.7%**
ITT	IGA 0/1	937	273	664	374	101	**15.2%**
PBS	EASI-50	172	59	113	114	55	**48.7%**
PBS	DLQI ≥ 4 point	172	105	67	114	9	**13.4%**
PBS	Composite	172	45	127	87	42	**33.1%**

Source: Table 1, p2 of the PSCR

AD = atopic dermatitis; DLQI = Dermatology Life Quality Index; EASI = Eczema Area and Severity Index; IGA = Investigator's Global Assessment; ITT = intent to treat; LTE = long-term extension; NEMO = nemolizumab; PBS = Pharmaceutical Benefits Scheme; PGA = Physician's Global Assessment

* Calculated as additional responders in LTE divided by those patients who entered LTE following treatment with NEMO in ARCADIA 1 or 2 as non-responders

** Subgroup population with severe AD only defined as an EASI score ≥ 20 and an PGA/IGA score of 4

6.22 The PSCR stated that an additional 8 weeks of Q4W treatment with NEMO is expected to result in an additional 30.1% of ITT patients demonstrating an EASI 75 response and 9.6% demonstrating an IGA 0/1 response, and an additional 34.5% of patients in the severe AD PBS population demonstrating an EASI 50 response. The PSCR stated that this supported the request for an extended induction treatment phase.

6.23 Table 10 presents an analysis of the proportion of patients achieving relevant efficacy outcomes with an additional 8 weeks of NEMO Q4W, that is, an extended induction of 24 weeks. The PSCR applied the response rates at Week 8 in patients who entered the LTE as non-responders after receiving NEMO for 16 weeks in ARCADIA 1 and ARCADIA 2 (see Table 9) to the expected cohort of non-responders in ARCADIA 1 and ARCADIA 2 to estimate the total response rate at Week 24.

Table 10: Naïve comparison of NEMO 24 weeks (16 + 8) and DUPI 16 weeks response rates

		NEMO Week 16 from trial				Additional 8 weeks (i.e. up to 24 weeks initial period)			DUPI response at 16 weeks*
Pop	Outcome	n	N	% response	Non-responders in ARCADIA 1&2, n	% additional response from LTE**	Expected total responders after 24 weeks, n	Total NEMO response at 24 weeks	
ITT	EASI-75	490	1,142	42.9%	652	30.1%	686	60.1%	64.2%
ITT	IGA 0/1	418	1,142	36.6%	724	9.6%	488	42.7%	38.2%
PBS***	EASI-50	164	330	49.7%	166	34.5%	221	67.1%	67.0%

Source: Table2, p3 of the PSCR

AD = atopic dermatitis; DUPI = dupilumab; EASI = Eczema Area and Severity Index; IGA = Investigator's Global Assessment; ITT = intent to treat; LTE = long-term extension; NEMO = nemolizumab; PBS = Pharmaceutical Benefits Scheme; PGA = Physician's Global Assessment

* Derived from LEB PSD, March 2024 PBAC meeting

** Calculated as additional responders in LTE divided by those patients who entered LTE following treatment with NEMO in ARCADIA 1 or 2 as non-responders

*** Subgroup population with severe AD only defined as an EASI score ≥ 20 and an PGA/IGA score of 4

6.24 Following an extended induction for non-responders at Week 16, the PSCR stated that NEMO at Week 24 was at least as effective as DUPI at Week 16.

6.25 Table 11 presents an analysis of the proportion of patients achieving relevant efficacy outcomes with an additional 20 weeks of NEMO Q4W, that is, induction extended to 36 weeks. The PSCR applied the response rates at Week 20 in patients who entered the LTE as non-responders after receiving NEMO for 16 weeks in ARCADIA 1 and ARCADIA 2 to the cohort of non-responders in ARCADIA 1 and ARCADIA 2 to estimate the total response rate at Week 36 in the severe PBS population. The PSCR stated that as expected, NEMO response at Week 36 is higher than NEMO response at Week 24. The PSCR stated that the additional 20-week data is provided as a confirmatory analysis.

Table 11: Naïve comparison of NEMO 36 weeks (16 + 20) and DUPI 16 weeks response rates

		NEMO Week 16 from trial				Additional 20 weeks (i.e. up to 36 weeks initial period)			DUPI response at 16 weeks*
Pop	Outcome	n	N	% response	Non-responders from ARCADIA, n	% additional response from LTE**	Expected total responders after 36 weeks, n	Total NEMO response at 36 weeks	
ITT	EASI-75	490	1,142	42.9%	652	36.7%	729	63.8%	64.2%
ITT	IGA 0/1	418	1,142	36.6%	724	15.2%	528	46.2%	38.2%
PBS***	EASI-50	164	330	49.7%	166	48.7%	245	74.2%	67.0%
PBS***	DLQI≥4 point	190	294	64.6%	104	13.4%	204	69.4%	68.9%
PBS***	Composite	130	294	44.2%	164	33.1%	184	62.7%	59.7%

Source: Table 3, p3 of the PSCR

AD = atopic dermatitis; DLQI = Dermatology Life Quality Index; DUPI = dupilumab; EASI = Eczema Area and Severity Index; IGA = Investigator's Global Assessment; ITT = intent to treat; LTE = long-term extension; NEMO = nemolizumab; PBS = Pharmaceutical Benefits Scheme; PGA = Physician's Global Assessment

* Derived from LEB PSD, March 2024 PBAC meeting

** Calculated as additional responders in LTE divided by those patients who entered LTE following treatment with NEMO in ARCADIA 1 or 2 as non-responders

*** Subgroup population with severe AD only defined as an EASI score ≥ 20 and an PGA/IGA score of 4

NEMO versus placebo in the subgroup of patients with severe AD

6.26 The requested listing for NEMO was restricted to patients with severe AD only, which was defined as IGA = 4 and EASI ≥ 20 at baseline. Results for the severe AD subgroups of the NEMO trials, as per the definition in the PBS listing, are presented in Table 12 to Table 14, for the composite endpoint of EASI-50 and ≥ 4-point improvement in DLQI and its component outcomes.

Table 12: Pooled results for NEMO 30 mg Q4W vs placebo: EASI-50 at Week 16 – PBS population

	NEMO 30 mg Q4W n/N (%)	Placebo n/N (%)	RR (95% CI)	RD (95% CI)
ARCADIA 1	90/173 (52.0)	36/80 (45.0)	1.16 (0.87, 1.53)	0.07 (-0.06, 0.20)
ARCADIA 2	74/157 (47.1)	20/78 (25.6)	**1.84 (1.22, 2.78)**	**0.22 (0.09, 0.34)**
Study 114322	26/46 (56.5)	4/17 (23.5)	2.40 (0.98, 5.87)	0.33 (0.08, 0.58)
Pooled (REM)			**1.55 (1.01, 2.37)**	**0.18 (0.05, 0.32)**

Source: Table 2-89, p217 of the submission.

CI = confidence interval; EASI-50 = proportion of patients with ≥ 50% improvement in Eczema Area and Severity Index from baseline; NEMO = nemolizumab; Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk

Bold = statistically significant.

Table 13: Pooled results for NEMO 30 mg Q4W vs placebo: ≥ 4-point improvement in DLQI at Week 16 – PBS population

	MENO 30 mg Q4W n/N (%)	Placebo n/N (%)	RR (95% CI)	RD (95% CI)
ARCADIA 1	115/173 (66.5)	43/80 (53.8)	1.24 (0.98, 1.56)[a]	0.13 (-0.00, 0.26)[a]
ARCADIA 2	99/157 (63.1)	34/78 (43.6)	**1.45 (1.09, 1.91)[a]**	**0.19 (0.06, 0.33)[a]**
Study 114322[b]	27/46 (58.7)	7/17 (41.2)	1.43 (0.77, 2.64)	0.18 (-0.10, 0.45)
Pooled (REM)			**1.33 (1.12, 1.57)[a]**	0.16 (0.07, 0.25)[a]

Source: Table 2-72, p204 of the submission.

CI = confidence interval; NEMO = nemolizumab, RD = risk difference; DLQI = Dermatology Life Quality Index; Q4W = every 4 weeks; REM = random effects model; RR = relative risk

Bold = statistically significant.

[a] Results calculated during the evaluation, using STATA 15.

[b] Results for the outcome of ≥4-point improvement in DLQI were reported at Week 12 for Study 114322

Table 14: Pooled results for NEMO 30 mg Q4W vs placebo: composite outcome of EASI-50 and ≥ 4-point improvement in DLQI at Week 16 – PBS population

	NEMO 30 mg Q4W n/N (%)	Placebo n/N (%)	RR (95% CI)	RD (95% CI)
ARCADIA 1	74/162 (45.7)	26/71 (36.6)	1.25 (0.88, 1.77)	0.09 (-0.05, 0.23)
ARCADIA 2	56/132 (42.4)	10/70 (14.3)	2.97 (1.62, 5.45)	0.28 (0.16, 0.40)
Study 114322[a]	21/46 (45.7)	3/17 (17.6)	2.59 (0.88, 7.57)	0.28 (0.05, 0.51)
Pooled (REM)			**1.98 (1.00, 3.92)**	**0.21 (0.07,0.35)**

Source: Nemolizumab PBAC submission error 6 May 2025.

CI = confidence interval; DLQI = Dermatology Life Quality Index; EASI-50 = proportion of patients with ≥ 50% improvement in Eczema Area and Severity Index from baseline; NEMO = nemolizumab, Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk

Bold = statistically significant.

[a] Results for the outcome of ≥ 4-point improvement in DLQI were reported at Week 12 for Study 114322

6.27 For both components of the composite endpoint, the pooled results showed that NEMO was associated with a statistically significant improvement in EASI-50 (RR = 1.55, 95% CI: 1.01, 2.37) and 4-point improvement in DLQI (RR = 1.33, 95% CI: 1.12, 1.57), compared with placebo.

6.28 The composite outcome of EASI-50 and ≥ 4-point improvement in DLQI is the PBAC preferred outcome for the assessment of severe AD and is also the definition of treatment response specified in the continuing listings for NEMO and DUPI. The treatment effect of NEMO for this composite endpoint was inconsistent across the severe AD subgroups in NEMO trials, with a RR of 1.25 (95% CI: 0.88, 1.77) in ARCADIA 1 and 2.97 (95% CI: 1.62, 5.45) in ARCADIA 2. However, the pooled result did show a statistically significant difference between NEMO and placebo for the treatment of severe AD (RR = 1.98; 95% CI: 1.00, 3.92). Of note, the proportion of patients who achieved ≥ 4-point improvement in DLQI and the proportion of responders who achieved both EASI-50 and ≥ 4-point improvement in DLQI were calculated post hoc based on patient level data from NEMO trials for the purpose of the submission. The interpretation of the composite outcome should consider the heterogeneity in the event rate across the placebo arms of the NEMO trials (36.6% in ARCADIA 1 vs. 14.3% in ARCADIA 2 vs. 17.6% in Study 114322), which may suggest different baseline risks for patients in the trials.

6.29 An ITC was not carried out to compare the severe AD subgroup of the NEMO trials to the severe AD subgroup of the DUPI trials, due to the lack subgroup data from the included DUPI trials.

6.30 No evidence was provided in the submission to demonstrate the efficacy of NEMO for the treatment of severe AD affecting the face and/or hands only.

Comparative harms

NEMO versus placebo

6.31 Table 15 displays the treatment-emergent adverse events (TEAEs) reported during the initial treatment period across the NEMO trials.

Table 15: Summary of TEAEs in the NEMO trials – initial treatment period[a] (safety population)

	ARCADIA 1		ARCADIA 2		ARCADIA CYCLO		Study 114322	
	NEMO 30 mg Q4W N = 616	Placebo N = 321	NEMO 30 mg Q4W N = 519	Placebo N = 263	NEMO 30 mg Q4W N = 137	Placebo N = 137	NEMO 30 mg Q4W N = 55	Placebo N = 57
TEAE	306 (49.7)	146 (45.5)	215 (41.4)	117 (44.5)	71 (51.8)	70 (51.1)	47 (82.5)	43 (76.8)
TEAE by maximum severity								
Mild	168 (27.3)	89 (27.7)	113 (21.8)	66 (25.1)	27 (19.7)	35 (25.5)	NR	NR
Moderate	120 (19.5)	49 (15.3)	81 (15.6)	44 (16.7)	42 (30.7)	33 (24.1)	NR	NR
Severe	18 (2.9)	8 (2.5)	21 (4.0)	7 (2.7)	2 (1.5)	2 (1.5)	NR	NR
Study drug-related TEAE[a]	123 (20.0)	42 (13.1)	67 (12.9)	29 (11.0)	13 (9.5)	15 (10.9)	NR	NR
Study drug-related TEAE by maximum severity[b,c]								
Mild	78 (12.7)	30 (9.3)	29 (5.6)	15 (5.7)	NR	NR	NR	NR
Moderate	38 (6.2)	10 (3.1)	31 (6.0)	11 (4.2)	NR	NR	NR	NR
Severe	7 (1.1)	2 (0.6)	7 (1.3)	3 (1.1)		NR	NR	NR
TEAE related to protocol procedure[d]	33 (5.4)	9 (2.8)	14 (2.7)	6 (2.3)	0	2 (1.5)	NR	NR
SAE	6 (1.0)	4 (1.2)	13 (2.5)	3 (1.1)	3 (2.2)	2 (1.5)	2 (3.5)	1 (1.8)
SAE related to study drug	0	0	5 (1.0)	0	1 (0.7)	1 (0.7)	NR	NR
TEAE leading to study drug withdrawal	11 (1.8)	13 (4.0)	18 (3.5)	3 (1.1)	3 (2.2)	3 (2.2)	NR	NR
TEAE leading to study discontinuation	9 (1.5)	3 (0.9)	15 (2.9)	3 (1.1)	2 (1.5)	3 (2.2)	2 (3.5)	4 (7.0)
Treatment-emergent AESIs	56 (9.1)	20 (6.2)	47 (9.1)	21 (8.0)	18 (13.1)	6 (4.4)	NR	NR
TEAE leading to death	0	0	0	0	0	0	0	0

Source: Table 2-51, p169, Table 2-59, p181, and Table 2-60, p182 of the submission.

AESIs = adverse events of special interest; NEMO = nemolizumab; Q4W = every 4 weeks; SAEs = serious adverse events; TEAEs = treatment-emergent adverse events

[a] Safety results were reported at Week 16 for ARCADIA 1, ARCADIA 2 and ARCADIA CYCLO, and at Week 24 for Study 114322.

[b] Study drug-related TEAEs were those for which a reasonable possibility of relationship was reported (or with a missing relationship).

[c] If subjects experienced multiple events, the subjects were counted once at the event with maximum severity.

[d] Including topical background therapy.

6.32 Compared with placebo, a higher proportion of patients in the NEMO group experienced drug-related TEAEs (20.0% vs. 13.1%) and TEAEs related to protocol procedure (including topical background therapy) (5.4% vs. 2.8%) in ARCADIA 1, serious adverse events (SAEs) (2.5% vs. 1.1%), TEAEs leading to study drug withdrawal (3.5% vs. 1.1%) and TEAEs leading to study discontinuation (2.9% vs. 1.1%) in ARCADIA 2, treatment-emergent adverse events of special interest (AESIs)[10] (13.1% vs. 4.4%) in ARCADIA CYCLO, and SAEs (3.5% vs. 1.8%) in Study 114322. Some of the differences were not statistically significant, as the trials were not statistically powered to detect a true difference.

6.33 In ARCADIA 1 the most common TEAE by system organ class reported at Week 16 was infections and infestations (18.3% for NEMO vs. 20.9% for placebo). This was also the

[10] AESIs included: injection related reactions, newly diagnosed asthma or worsening of asthma, infections, peripheral oedema, facial oedema, elevated alanine aminotransferase or aspartate aminotransferase (>3 upper limit of normal in combination with elevated bilirubin (> 2 upper limit of normal).

most common TEAEs in ARCADIA 2 (17.0% vs. 20.2%), ARCADIA CYCLO (32.1% vs. 27.7%), and Study 114322 (59.6% vs. 42.9%). The difference between the arms in Study 114322 was heavily driven by the rate of upper respiratory tract infections reported in the NEMO arm (10.5% vs. 1.8%). Dermatitis atopic was the most commonly reported TEAE by preferred term in ARCADIA 1 (12.2% for NEMO vs. 10.6% for placebo) and ARCADIA 2 (7.1% vs. 5.7%), and this was also the common TEAE in ARCADIA CYCLO (7.3% vs. 4.4%) and Study 114322 (24.6% vs. 32.1%).

6.34 Table 16 provides a summary of TEAEs during the maintenance period of ARCADIA 1 and ARCADIA 2 up to Week 48.

Table 16: Overall summary of TEAEs during the maintenance treatment period – ARCADIA 1 and ARCADIA 2 (enrolled safety subjects in the maintenance period population)

	ARCADIA 1				ARCADIA 2			
Treatment in ITP	**NEMO 30 mg Q4W**			**Placebo**	**NEMO 30 mg Q4W**			**Placebo**
Treatment in MTP	**NEMO 30 mg Q8W N = 90**	**NEMO 30 mg Q4W N = 91**	**Placebo N = 91**	**Placebo[b] N = 100**	**NEMO 30 mg Q8W N = 77**	**NEMO 30 mg Q4W N = 79**	**Placebo N = 77**	**Placebo[b] N = 84**
TEAE	50 (55.6)	53 (58.2)	53 (58.2)	55 (55.0)	40 (51.9)	38 (48.1)	45 (58.4)	37 (44.0)
TEAE by maximum severity								
Mild	24 (26.7)	27 (29.7)	30 (33.0)	36 (36.0)	24 (31.2)	20 (25.3)	22 (28.6)	19 (22.6)
Moderate	22 (24.4)	22 (24.2)	20 (22.0)	18 (18.0)	14 (18.2)	17 (21.5)	21 (27.3)	17 (20.2)
Severe	4 (4.4)	4 (4.4)	3 (3.3)	1 (1.0)	2 (2.6)	1 (1.3)	2 (2.6)	1 (1.2)
Study drug-related TEAE[a]	15 (16.7)	10 (11.0)	9 (9.9)	11 (11.0)	5 (6.5)	8 (10.1)	9 (11.7)	3 (3.6)
Study drug-related TEAE by maximum severity[a,b]								
Mild	7 (7.8)	6 (6.6)	6 (6.6)	10 (10.0)	1 (1.3)	3 (3.8)	3 (3.9)	1 (1.2)
Moderate	8 (8.9)	3 (3.3)	3 (3.3)	1 (1.0)	4 (5.2)	5 (6.3)	4 (5.2)	2 (2.4)
Severe	0	1 (1.1)	0	0	0	0	2 (2.6)	0
TEAE related to protocol procedure[c]	5 (5.6)	2 (2.2)	2 (2.2)	3 (3.0)	1 (1.3)	2 (2.5)	1 (1.3)	2 (2.4)
SAE	3 (3.3)	4 (4.4)	2 (2.2)	1 (1.0)	0	6 (7.6)	2 (2.6)	1 (1.2)
SAE related to study drug	0	0	0	0	0	1 (1.3)	1 (1.3)	0
TEAE leading to study drug withdrawal	3 (3.3)	1 (1.1)	2 (2.2)	2 (2.0)	2 (2.6)	3 (3.8)	3 (3.9)	2 (2.4)
TEAE leading to study discontinuation	3 (3.3)	0	1 (1.1)	1 (1.0)	2 (2.6)	3 (3.8)	3 (3.9)	1 (1.2)
Treatment-emergent AESIs	18 (20.0)	16 (17.6)	14 (15.4)	15 (15.0)	7 (9.1)	8 (10.1)	17 (22.1)	9 (10.7)
TEAE leading to death	0	0	0	0	0	0	0	0

Source: Table 2-52, pp171-172

AEs = adverse events; AESIs = adverse events of special interest; ITP = initial treatment period; MTP = maintenance treatment period; NEMO = nemolizumab; Q4W = every 4 weeks; Q8W = every 8 weeks; SAEs = serious adverse events; TEAEs = treatment-emergent adverse events

[a]. Study drug-related TEAEs were those for which a reasonable possibility of relationship was reported (or with a missing relationship).

[b]. If subjects experienced multiple events, the subjects were counted once at the event with maximum severity.

[c] Including topical background therapy.

Note: Percentages were based on the number of subjects in each treatment group. Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 25.0. The Initial Treatment Period was defined as the period from start of treatment up to and including Week 16. For each row category, a subject with 2 or more AEs in that category was counted only once.

6.35 In the ARCADIA 1 maintenance period, patients treated with NEMO 30 mg Q8W, in comparison to placebo, reported a higher incidence of study drug-related TEAEs (16.7% vs. 11.0%), severe TEAEs (4.4% vs. 1.0%), SAEs (3.3% vs. 1.0%), TEAEs leading to study discontinuation (3.3% vs. 1.0%), and treatment-emergent AESIs (20.0% vs. 15.0%). In ARCADIA 2, a higher proportion of patients treated with NEMO 30mg Q8W, in comparison to placebo, reported any TEAEs (51.9% vs. 44.0%) and study drug-related TEAEs (6.5% vs. 3.6%), and TEAEs leading to study discontinuation (2.6% vs. 1.2%). Again, dermatitis atopic was the most common TEAE by preferred term during

the maintenance treatment period for both NEMO and placebo (12.2% vs. 10.6% in ARCADIA 1; 7.1% vs. 5.7% in ARCADIA 2), followed by headache (4.5% vs. 3.4% in ARCADIA 1; 3.5% vs. 3.8% in ARCADIA 2) and asthma (5.4% vs. 4.1% in ARCADIA 1; 2.1% vs. 2.7% in ARCADIA 2). No notable differences were observed between treatment arms for these common TEAEs.

ITCs of NEMO versus DUPI

6.36 Table 17 presents a summary of the key safety outcomes used to inform the ITCs of NEMO versus DUPI.

Table 17: ITCs of NEMO 30 mg Q4W vs DUPI 300 mg Q2W: TEAEs, serious TEAEs and TEAEs leading to discontinuation (Safety population)[a]

	Intervention n/N (%)	Comparator n/N (%)	RR (95% CI)	RD (95% CI)
Any TEAEs				
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	306/616 (49.7)	146/321 (45.5)	1.09 (0.95, 1.26)	0.04 (-0.03, 0.11)
ARCADIA 2	215/519 (41.4)	117/263 (44.5)	0.93 (0.79, 1.10)	-0.03 (-0.10, 0.04)
Study 114322	47/57 (82.5)	43/57 (76.8)	1.09 (0.90, 1.32)	0.07 (-0.08, 0.22)
ARCADIA CYCLO	71/137 (51.8)	70/137 (51.1)	1.01 (0.81, 1.28)	0.01 (-0.11, 0.13)
Pooled (REM)			1.04 (0.94, 1.15)	0.02 (-0.04, 0.07)
DUPI 300 mg Q2W vs placebo				
CAFÉ	77/107 (72.0)	75/108 (69.4)	1.04 (0.87, 1.23)	0.03 (-0.10, 0.15)
CHRONOS	97/110 (88.2)	266/315 (84.4)	1.04 (0.96, 1.14)	0.04 (-0.04, 0.11)
JADE COMPARE	121/242 (50.0)	70/131 (53.4)	0.94 (0.76, 1.15)	-0.03 (-0.14, 0.07)
Pooled (REM)			1.03 (0.96, 1.10)	0.02 (-0.04, 0.07)
Indirect comparison				
NEMO 30 mg Q4W (pooled) vs DUPI 300 mg Q2W (pooled)			1.01 (0.90, 1.13)	-0.01 (-0.10, 0.08)
Serious TEAEs				
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	6/616 (1.0)	4/321 (1.2)	0.78 (0.22, 2.75)	-0.00 (-0.02, 0.01)
ARCADIA 2	13/519 (2.5)	3/263 (1.1)	2.20 (0.63, 7.64)	0.01 (-0.01, 0.03)
Study 114322	2/57 (3.5)	1/57 (1.8)	2.00 (0.187, 21.44)	0.02 (-0.04, 0.08)
ARCADIA CYCLO	2/137 (1.5)	2/137 (1.5)	1.00 (0.14, 7.00)	0.00 (-0.03, 0.03)
Pooled (REM)			1.32 (0.61, 2.83)	0.00 (-0.01, 0.01)
DUPI 300 mg Q2W vs placebo				
CAFÉ	2/107 (1.9)	2/108 (1.9)	1.01 (0.15, 7.04)	0.0 (-0.04, 0.04)
CHRONOS	4/110 (3.6)	16/315 (5.1)	0.72 (0.25, 2.10)	-0.01 (-0.06, 0.03)
JADE COMPARE	2/242 (0.8)	5/131 (3.8)	0.22 (0.04, 1.10)	-0.03 (-0.07, 0.01)
Pooled (REM)			0.56 (0.25, 1.27)	-0.02 (-0.04, 0.01)
Indirect comparison				
NEMO 30 mg Q4W (pooled) vs DUPI 300 mg Q2W (pooled)			2.36 (0.77, 7.21)	0.02 (-0.01, 0.05)
TEAEs leading to discontinuation				
NEMO 30 mg Q4W vs placebo				
ARCADIA 1	9/616 (1.5)	3/321 (0.9)	1.56 (0.43, 5.73)	0.01 (-0.01, 0.02)
ARCADIA 2	15/519 (2.9)	3/263 (1.1)	2.53 (0.74, 8.68)	0.02 (-0.00, 0.04)
Study 114322	2/57 (3.5)	4/57 (7.0)	0.50 (0.10, 2.62)	-0.04 (-0.12, 0.05)
ARCADIA CYCLO	2/137 (1.5)	3/137 (2.2)	0.67 (0.11, 3.93)	-0.01 (-0.04 0.02)
Pooled (REM)			1.30 (0.62, 2.66)	0.01 (0.00, 0.02)
DUPI 300 mg Q2W vs placebo				
CAFÉ	0/107	1/108 (0.9)		-0.01 (-0.03, 0.01)
CHRONOS	2/110 (1.8)	24/315 (7.6)	0.24 (0.06, 0.99)	-0.06 (-0.10, -0.02)
JADE COMPARE	8/242 (3.3)	5 /131(3.8)	0.87 (0.29, 2.59)	-0.01 (-0.05, 0.04)
Pooled (REM)			0.51 (0.21, 1.25)	-0.02 (-0.06, 0.01)
Indirect comparison				
NEMO 30 mg Q4W (pooled) vs DUPI 300 mg Q2W (pooled)			2.53 (0.80, 8.00)	0.03 (-0.00, 0.06)

Source: Table 2-88, p 215 of the submission.

CI = confidence interval; DUPI = dupilumab; ITC = indirect treatment comparison; Q2W = every 2 weeks; Q4W = every 4 weeks; RD = risk difference; REM = random effects model; RR = relative risk; TEAEs = treatment emergent adverse events

[a] Treatment exposure was 16 weeks for ARCADIA 1, ARCADIA 2, ARCADIA CYCLO, CAFÉ and COMPARE, 24 weeks for Study 114322, and 52 weeks for CHRONOS

Blue shading indicates data previously seen by the PBAC

6.37 For all the safety outcomes included in the ITCs, i.e. any TEAEs, SAEs, and TEAEs leading to discontinuation, there were no statistically significant differences observed between either NEMO or DUPI in comparison to placebo. The ITC showed similar safety between NEMO and DUPI in terms of any TEAEs (RR = 1.01, 95% CI: 0.90, 1.13). However, the wide 95% confidence intervals in the ITCs for SAEs (RR = 2.36, 95% CI: 0.77, 7.21) and TEAEs leading to discontinuation (RR = 2.53, 95% CI: 0.80, 8.00) indicated that the analyses were not adequately powered to detect differences in these outcomes. Further, the small event numbers for some of the outcomes make the results difficult to interpret. Other limitations relating to the safety ITCs included the limited safety outcomes included in the ITCs, the various duration of treatment across studies (e.g. 16 weeks in ARCADIA 1, ARCADIA 2, ARCADIA CYCLO, CAFÉ, and JADE COMPARE vs. 52 weeks in CHRONOS) and the short time frames of safety data included in the ITC for NEMO (16-24 weeks) relative to its expected long term use in clinical practice.

6.38 The PBAC has previously considered that DUPI was inferior compared to placebo (representing standard of care) in terms of safety due to the increased incidence of conjunctivitis and injection site reactions (paragraph 7.11, dupilumab PSD, March 2020 PBAC meeting). No formal ITCs of this outcome were performed. There were no reported differences in the rate of conjunctivitis between the NEMO and placebo arms of the NEMO trials.

Benefits/harms

6.39 A benefits and harms table was not presented as the submission made a claim of non-inferiority.

Clinical claim

6.40 The submission described NEMO as non-inferior in terms of effectiveness compared with DUPI and non-inferior in terms of safety compared to DUPI for the treatment of chronic severe AD in patients who are inadequately controlled on topical therapies. In addition, the submission claimed that NEMO offers the benefits of fewer injections and reduced rate of conjunctivitis, compared to DUPI.

6.41 The ESC considered that the claim of non-inferior efficacy was not supported by the evidence presented in the submission and the PSCR. Further, the ESC noted that no comparative data between NEMO and its main comparator, DUPI, was presented in the proposed PBS target population of patients with severe AD. Overall, the ESC considered that NEMO was inferior in terms of clinical efficacy compared to DUPI, based on the results of the ITCs for patients with moderate to severe AD with the differences statistically significantly in favour of DUPI for both EASI-75 (RR = 0.61; 95% CI: 0.41, 0.89) and IGA success (RR = 0.49; 95% CI: 0.34, 0.69), the two primary endpoints in the submission.

6.42 The ESC noted that the PSCR presented additional analyses of the LTE study which included comparison of NEMO Q4W at Week 24 and Week 36 to DUPI at Week 16. The ESC considered a longer induction period and longer treatment duration appeared

to demonstrate improvements with NEMO in comparison to placebo. However, the ESC considered that the results did not provide support to the submission's clinical claim of non-inferior effectiveness versus DUPI given the comparison did not consider response rates at comparable times (24 to 36 weeks for NEMO and 16 weeks for DUPI), the unanchored nature of the comparisons and the transitivity issues discussed above. Further, the ESC noted that the extended induction regimen was not included in the PI for NEMO. The Pre-PBAC response reiterated that the additional analyses of the LTE study provided with the PSCR recognises that, for some patients, a longer induction period may be required to achieve a comparable response to induction with DUPI (at Week 16). Additionally, the Pre-PBAC response stated that any uncertainty with respect to clinical efficacy is mitigated by the continuation criteria in the proposed restriction that specifically limits maintenance treatment to responders.

6.43 The ESC noted that a recent network meta-analysis[11]concluded that for relative efficacy comparisons up to 16 weeks of treatment "nemolizumab probably has lower efficacy than dupilumab with regard to change in EASI, patient-orientated eczema measure (POEM) and DLQI, but similar efficacy with regard to peak pruritus numeric rating scale (PP-NRS)".

6.44 The ESC noted that in the pooled data for the severe AD subgroup, no significant difference was observed between NEMO and placebo in the composite outcome of EASI-50 and 4-point improvement in DLQI (RR = 1.47, 95% CI: 0.65, 3.33), however the confidence intervals were wide.

6.45 The ESC considered, in line with the ACM advice, that NEMO could potentially provide an alternative option for patients who don't respond completely to DUPI or those who cannot tolerate its adverse effects.

6.46 The ESC considered that the therapeutic conclusion of non-inferior safety was uncertain. Although the ITC showed similar safety of NEMO and DUPI in terms of TEAEs, the ITCs for serious TEAEs and TEAEs leading to discontinuation were statistically underpowered, indicated by the wide 95% confidence intervals of the indirect results. In addition, the selected safety outcomes in the ITCs, namely any TEAEs, serious TEAEs, TEAEs leading to discontinuation, may not allow for a meaningful comparison of NEMO and DUPI as they do not capture individual AEs that may be important, such as the increased risk of conjunctivitis with DUPI. Additionally, any interpretation of the ITC results for safety should consider the short duration of treatment (at Week 16) and the transitivity of NEMO and DUPI trials indirectly compared.

6.47 The PBAC considered that the claim of non-inferior comparative effectiveness was not adequately supported by the presented data and a claim of inferior comparative effectiveness would be more reasonable.

6.48 The PBAC considered the claim of non-inferior comparative safety to be uncertain

[11] Drucker, AM. et al. Living network meta-analysis to compare nemolizumab against other available targeted systemic treatments for atopic dermatitis. *The British Journal of Dermatology.* 2025;May 7:ljaf166.

noting it was based on ITCs which were statistically underpowered and the selected safety outcomes in the ITCs did not capture individual AEs that may be important when comparing NEMO to DUPI. However, the PBAC noted that both NEMO and DUPI did not report statistically significant differences to placebo in terms of TEAEs or SAEs leading to discontinuation (see paragraph 6.37).

Economic analysis

6.49 The submission presented a CMA comparing NEMO with DUPI for the treatment of chronic severe AD based on a claim of non-inferior effectiveness and safety compared to DUPI, but with fewer injection site reactions and incidences of conjunctivitis. The CMA relies on the claim of non-inferior efficacy of NEMO compared to DUPI. The ESC considered that NEMO was likely inferior compared to DUPI. The key assumptions and components of the cost-minimisation approach are summarised in Table 18.

Table 18: Key components and assumptions of the CMA

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on evidence presented in the submission, effectiveness is assumed to be non-inferior. The ESC considered that NEMO was inferior to DUPI in terms of effectiveness.
Therapeutic claim: safety	Based on evidence presented in the submission, safety is assumed to be non-inferior, but with fewer injection site reactions and patients with conjunctivitis. The ESC considered that the claim of non-inferior safety was uncertain and noted that the submission did not present ITCs for injection site reactions or conjunctivitis versus DUPI.
Evidence base	Indirect treatment comparison of nemolizumab and dupilumab
Equi-effective doses	Nemolizumab initial dose of 60 mg SC, followed by 30 mg Q4W SC for 16 weeks and 30 mg Q8W SC thereafter = dupilumab 600 mg SC injection loading dose, followed by 300 mg SC injection Q2W in adult patients and adolescents weighing ≥ 60 kg; 400 mg SC injection loading dose, followed by 200 mg SC injection Q2W in adolescents weighing < 60 kg.
Direct medicine costs	The cost of nemolizumab per patient for two years of treatment is higher to account for a reduction in conjunctivitis in patients treated with nemolizumab compared to those treated with dupilumab.
Cost offsets	Additional cost to account for a reduction in the adverse events relating to conjunctivitis.

Source: Table 3-1, pp229-230 of the submission.
CMA = cost-minimisation approach; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous

6.50 The submission proposed the equi-effective doses as follows:

- For adults and adolescents ≥ 60kg; NEMO at an initial dose of 60 mg (given as 2 x 30 mg SC injections at week 0), followed by 30 mg SC injection Q4W until week 16 and 30 mg Q8W thereafter is equi-effective to DUPI 600 mg SC injection as a loading dose followed by 300 mg SC injection Q2W.
- For adolescents < 60kg; NEMO at an initial dose of 60 mg (given as 2 x 30 mg SC injections at week 0), followed by 30 mg subcutaneous SC injection Q4W until week 16 and 30 mg Q8W thereafter is equi-effective to DUPI 400 mg SC injection as a loading dose followed by 200 mg SC injection Q2W.

The submission did not consider relative dose intensity (RDI) in the CMA. The RDI in the ARCADIA trials for NEMO was 96% while that of DUPI in JADE COMPARE was 93.4%.

6.51 In addition to direct medicine costs, the submission included cost offsets of $0.71 per patient per week (resulting in a total cost of $73.93 across the two years), associated with a reduction in the number of eye complications associated with DUPI over the first 16 weeks of treatment. This approach assumed that the incidence of eye complications observed during the first 16 weeks in the DUPI trials would continue to apply over the 2-year treatment period. No long-term data were presented to support this assumption, noting these costs were not included in previous submissions of treatments for AD made to the PBAC (abrocitinib PSD, November 2024 PBAC Meeting; upadacitinib PSD, July 2021 PBAC Meeting and lebrikizumab PSD, March 2024 PBAC meeting). The PSCR maintained these cost offsets were appropriate, given NEMO does not result in ocular AEs. The ESC considered that cost offsets for conjunctivitis should not be included in the CMA.

6.52 The results of the CMA are presented below. Of note, DUPI is subject to flat pricing, i.e., the published prices for both the 200 mg and 300 mg doses are the same.

Table 19: Cost-minimisation of NEMO against DUPI (based on published prices)

Component	Nemolizumab	Dupilumab
AEMP/EMP per script	$2,670	$1,609.86
No. of doses over 2 years	16	53
No. of scripts over 2 years	16	26.5
Total medicines cost over 2 years	$42,735.22	$42,661.29
Cost of managing eye complications	$0.00	$73.93
Total 2-year treatment cost	$42,735.22	$42,735.22
DPMQ	$2,833.55	$1,755.66

Source: tabulated during the evaluation, from Table 3-4, p235 of the submission.
AEMP = approved ex-manufacturer price; DPMQ = dispensed price for maximum quantity; DUPI = dupilumab; NEMO = nemolizumab; No. = number

6.53 The cost offsets associated with managing eye complications are uncertain. If the costs associated with conjunctivitis are applied for only a 16-week period, the total 2-year treatment cost reduces, resulting in a lower EMP of $2,667.04 per NEMO script. If costs associated with conjunctivitis are excluded entirely, the resulting EMP is $2,666.33 per NEMO script. If RDI is considered (96% for NEMO and 93.4% for DUPI), the EMP reduces to $2,598.83 per NEMO script.

6.54 The PSCR presented a revised CMA which included an extended induction period for patients who had not responded to NEMO at 16 weeks. For these patients an additional injection of NEMO is required before progression to the continuation stage of treatment. The PSCR calculated, based on the composite outcome of EASI-50 in the PBS population, that 74.1% (164/221) of responders will receive 16 injections over 2 years and 25.9% (57/221) will require the extended induction and will receive 17 injections. This resulted in an increase in the weighted number of injections to 16.26 over 2 years and a revised proposed published EMP per injection of $2,628.42 (reduced by 1.6% from $2,670.95). As noted above, the ESC considered that the

extended induction period was not appropriate as it was not included in the approved PI. The Pre-PBAC response proposed a further price reduction of [redacted]%, resulting in an AEMP of $[redacted] to reduce any further uncertainty regarding the non-inferiority clinical claim.

6.55 Key uncertainties of the CMA relate to long term comparative effectiveness and safety of NEMO vs DUPI. The ESC considered that NEMO was inferior in terms of clinical efficacy compared to DUPI. The ESC recalled that the PBAC had stated in its consideration of baricitinib for the same indication that "the literature suggests higher willingness to accept (WTA) for south-west quadrant incremental cost effectiveness ratio (ICERs) (where treatments are less effective and less costly) compared to willingness to pay (WTP) for north-east quadrant ICERs (where treatments are more effective and more costly)" (paragraph 7.13, baricitinib PSD, July 2021 PBAC meeting). The ESC considered that the price of NEMO should reflect this lower efficacy.

Drug cost/patient/year

6.56 Based on the results of the CMA from the submission, the drug cost/patient/dose for NEMO was $5,504.50 for the loading dose (60 mg) and $2,833.50 for the subsequent doses (30 mg Q4W, 30 mg Q8W). This results in a drug cost/patient/year for NEMO of $27,848 in Year 1 and $17,001 for each subsequent year.

6.57 The drug cost/patient/year for DUPI is $23,701 in Year 1 and $22,829 for each subsequent year.

Estimated PBS usage & financial implications

6.58 This submission was not considered by DUSC. The submission utilised a market-share approach to estimate the extent of use and financial impact of listing NEMO for the treatment of chronic severe AD. The key inputs for the financial analysis are summarised in Table 20.

Table 20: Data sources and parameter values applied in the utilisation and financial estimates

Data	Value	Source	Comment
Size of the market			
Total services for all strengths of DUPI and UPA for atopic dermatitis	DUPI: 206,257 UPA: 30,192 Total: 236,449	Services Australia Utilisation statistics for PBS items: 12291X, 12292Y, 12827D, 12828E, 12829F, 12831H, 12835M and 12836N (January – December 2024).	This was reasonable.
Annual growth in prescriptions	Yr 1: 19.6% Yr 2: 16.4% Yr 3: 14.1% Yr 4: 12.3% Yr 5: 11.0% Yr 6: 9.9%	DUPI PSD (Table 6, July 2024 PBAC Meeting)	The submission assumed that the severe AD population would experience linear growth of 7,597 patients per year, consistent with the July 2024 DUPI PSD. In July 2024, the PBAC considered that the growth rate of AD would stabilise from Year 4 onwards. A reduction of 5% in the growth rate from year 4 onwards was recommended.

Data	Value	Source	Comment
Phase of treatment	DUPI: 18.5% initiating, 81.5% continuing UPA: 26% initiating, 76% continuing	DUPI: based on the proportion of initial scripts required for 2 years of treatment, i.e., 5 of 27 scripts would be required for initial treatment (5/27 = 18.5%) UPA: based on Services Australia utilisation statistics.	This approach assumes that all patients that initiate treatment with DUPI will complete initial treatment. The ESC considered that this might not be reasonable as only approximately 60% of DUPI patients respond to treatment.
Grandfathered NEMO patients	[redacted][1] patients	Grandfathered patients were assumed to be accounted for in the estimated size of the market estimations.	This was noted.
Treatment utilisation			
Proportion applicable to indication	100%	Assumption	This was reasonable.
Uptake rate	[redacted]-[redacted]%	Assumption	Noting that NEMO was inferior compared to DUPI in terms of effectiveness, the ESC considered that the uptake rates may be too high.
Substitution rates	NEMO : DUPI (initial) = 0.6 NEMO : DUPI (continuing) = 0.45 NEMO : UPA (initial) = 0.75 NEMO : UPA (continuing) = 0.45	Substitution rates were calculated based on the number of scripts required for initial treatment and continuing treatment over 2 years for NEMO, DUPI and UPA.	This was consistent with the dosing schedules for all medicines.
Costs			
NEMO	Initiating: $5,504.50 Continuing: $2,833.55	Requested published DPMQ	The appropriate mark-up fees were applied to the requested AEMP.
DUPI	200 mg, 300 mg: $1,755.66	PBS items 12291X, 12292Y	This was correct.
UPA	15 mg: $1,272.78 30 mg: $2,077.76	PBS items 12827D, 12828E, 12829F, 12831H, 12835M and 12836N.	This was correct.
MBS costs	GP attendance: $42.85 Specialist attendance: $82.10	Offsets associated with MBS items 23 and 106 were included based on the claim that NEMO reduces the number of conjunctivitis events in patients.	It is not appropriate to include cost offsets associated with GP and specialist visits as these are not likely to be realised.

Source: tabulated during the evaluation.
AD = atopic dermatitis; AEMP = approved ex-manufacturer price; DPMQ = dispensed price for maximum quantity; DUPI = dupilumab; GP = General practitioner; MBS = Medicare Benefits Schedule; NEMO = nemolizumab; PBS = Pharmaceutical Benefits Scheme; PSD = public summary document; RPBS = Repatriation Pharmaceutical Benefits Scheme; UPA = upadacitinib

The redacted values correspond to the following ranges:
[1] < 500

6.59 The submission projected a linear annual growth of the DUPI and UPA market size based on projections previously presented to the PBAC (Table 6, dupilumab PSD, July 2024 PBAC Meeting). In July 2024, the PBAC noted that the assumption of linear growth in the market from Year 4 onwards was not reasonable as the market was expected to stabilise. It was recommended that the growth rate be reduced by 5% from Year 4 onwards (Table 8, dupilumab PSD, July 2024 PBAC Meeting).

6.60 The submission assumed that the market share of NEMO would grow from [redacted]% in Year 1 to [redacted] in Year 6. Given the inferior efficacy of NEMO compared to DUPI and UPA, the ESC considered that the uptake of NEMO may be overestimated.

6.61 The total number of NEMO prescriptions was estimated based on calculated substitution rates for initial and continuing treatment. As DUPI has the same PBS item code for initial and continuing supply, the number of initial (assumed to be 18.5% of all scripts) and continuing (81.5%) prescriptions for DUPI were based on the recommended dosing schedule in which 5 of a total of 27 scripts required for a treatment period of 2 years, are for initial treatment with DUPI. The ESC noted that this approach assumes that all patients who initiate treatment with DUPI complete initial treatment and progress to continuing treatment, i.e. it does not account for patients that may not respond to initial treatment with DUPI and therefore, discontinue treatment, which was not a reasonable assumption as only approximately 60% of patients are reported to respond to initial DUPI treatment (Table 19, dupilumab PSD, March 2020 PBAC Meeting). As the substitution rate of NEMO to DUPI for initial treatment is likely higher than that for continuing treatment, the financial impact of NEMO to the PBS/RPBS may be underestimated. Further, the financial estimates are highly sensitive to the split between initial and continuing DUPI scripts. The ESC noted that if a split of 26% and 74% between initial and continuing scripts (based on UPA utilisation statistics) was applied to all DUPI scripts, the net cost of NEMO to the PBS/RPBS increased from a cost saving to a cost of approximately $10 million to < $20 million in Year 6. PBS data for DUPI by treatment phase could reduce the uncertainty in the financial impact associated with the listing of NEMO. The Pre-PBAC response disagreed with the ESC and stated that it is more likely that the proportion of initiating scripts of NEMO could be less than the assumptions in the estimates, not higher, based on the long term treatment duration of DUPI.

6.62 The PSCR stated that for Years 3 to 6 of the forward estimates, NEMO patients will require an average 6.75 injections per year, which is lower than the average of 8.13 per year (16.26 over two years) applied in the financial estimates due to the PBAC's preferred approach of pricing products over the first two years of listing. The PSCR stated that assuming NEMO has the same persistence as DUPI, a six-year saving of approximately $50 million to < $60 million would be possible. The ESC noted these estimates were based on the published prices for NEMO and DUPI.

6.63 A summary of the net financial implications for the PBS/RPBS is provided in Table 21**.**

Table 21: Estimated reduction in the cost to the PBS/RPBS

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use of NEMO						
DUPI (initial) [a]	[redacted]1	[redacted]2	[redacted]3	[redacted]4	[redacted]5	[redacted]6
DUPI (continuing)	[redacted]7	[redacted]7	[redacted]8	[redacted]8	[redacted]9	[redacted]9
UPA (initial) [b]	[redacted]10	[redacted]11	[redacted]11	[redacted]11	[redacted]11	[redacted]11
UPA (continuing)	[redacted]12	[redacted]13	[redacted]13	[redacted]1	[redacted]1	[redacted]2
Existing size of the market	[redacted]8	[redacted]9	[redacted]9	[redacted]14	[redacted]14	[redacted]15
Market share of NEMO	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
NEMO: DUPI (initial)	[redacted]16	[redacted]10	[redacted]11	[redacted]11	[redacted]11	[redacted]17
NEMO: DUPI (continuing)	[redacted]11	[redacted]17	[redacted]12	[redacted]1	[redacted]2	[redacted]3
NEMO: UPA (initial)	[redacted]16	[redacted]16	[redacted]16	[redacted]16	[redacted]16	[redacted]16
NEMO: UPA (continuing)	[redacted]16	[redacted]16	[redacted]10	[redacted]10	[redacted]10	[redacted]11
Total NEMO prescriptions [c]	[redacted]17	[redacted]12	[redacted]1	[redacted]3	[redacted]5	[redacted]6
Cost to PBS/RPBS less copayments ($) [d]	[redacted]18	[redacted]19	[redacted]19	[redacted]20	[redacted]21	[redacted]21
Reduction in use of DUPI and UPA						
DUPI (200 mg and 300 mg doses) scripts	-[redacted]12	-[redacted]2	-[redacted]5	-[redacted]6	-[redacted]6	-[redacted]6
UPA (15 g) scripts	-[redacted]16	-[redacted]10	-[redacted]10	-[redacted]11	-[redacted]11	-[redacted]11
UPA (30 g) scripts	-[redacted]16	-[redacted]16	-[redacted]10	-[redacted]10	-[redacted]11	-[redacted]11
Total reduction in scripts	-[redacted]13	-[redacted]3	-[redacted]6	-[redacted]6	-[redacted]6	-[redacted]7
Reduction in cost to PBS/RPBS less copayments (-$) [e]	[redacted]22	[redacted]22	[redacted]22	[redacted]22	[redacted]22	[redacted]22
Net financial implications						
Net cost to PBS/RPBS (-$)	[redacted]22	[redacted]22	[redacted]22	[redacted]22	[redacted]22	[redacted]22
Net cost to MBS (revised)($) [f]	[redacted]23	[redacted]23	[redacted]23	[redacted]23	[redacted]23	[redacted]23
Net cost to PBS/RPBS/MBS (-$)	[redacted]22	[redacted]22	[redacted]22	[redacted]22	[redacted]22	[redacted]22

Source: tabulated during the evaluation.

DUPI = dupilumab; MBS = Medicare Benefits Schedule; NEMO = nemolizumab; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; UPA = upadacitinib

[a] Assuming 18.5% of all DUPI scripts are for initial treatment.

[b] Based on PBS utilisation statistics for upadacitinib PBS services.

[c] Based on proposed market share and substitution rates of 0.60 for DUPI initial scripts, 0.45 for DUPI continuing scripts, 0.75 for UPA initial scripts and 0.45 for UPA continuing scripts.

[d] Based on DPMQs of $5,504.50 for initial scripts, $2,833.50 for continuing scripts; and a PBS/RPBS split of 99.39% and 0.61%.

[e] Based on DPMQs of $1,755.66 for DUPI (200 mg and 300 mg doses), $1,272.78 for UPA 15 g scripts and $2,077.76 for UPA 30 g scripts.

[f] MBS offsets revised during evaluation to $0 as cost offsets associated with GP and specialist visits are unlikely to be realised in clinical practice.

The redacted values correspond to the following ranges:

[1] 50,000 to < 60,000
[2] 60,000 to < 70,000
[3] 70,000 to < 80,000
[4] 80,000 to < 90,000
[5] 90,000 to < 100,000
[6] 100,000 to < 200,000
[7] 200,000 to < 300,000
[8] 300,000 to < 400,000
[9] 400,000 to < 500,000
[10] 5,000 to < 10,000
[11] 10,000 to < 20,000
[12] 30,000 to < 40,000
13 40,000 to < 50,000

[14] 500,000 to < 600,000
[15] 600,000 to < 700,000
[16] 500 to < 5,000
[17] 20,000 to < 30,000
[18] $70 million to < $80 million
[19] $100 million to < $200 million
[20] $200 million to < $300 million
[21] $300 million to < $400 million
[22] net cost saving
[23] $0 to < $10 million

6.64 The submission estimated cost savings to the PBS/RPBS of $0 to < $10 million in Year 1, increasing to $10 million to < $20 million in Year 6, and totalling $40 million to < $50 million across the first 6 years.

6.65 The financial estimates presented in the submission included a reduction in costs to the MBS due to reduction in the number of eye complications associated with DUPI treatment. Costs for GP visits and specialist visits, using MBS items 23 and 106, were included. As cost offsets associated with GP and specialist visits unlikely to be realised, they were excluded from the calculations above.

Financial Management – Risk Sharing Arrangements

6.66 The submission did not propose a risk-sharing arrangement (RSA). An RSA is currently in place for DUPI and UPA.

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

7 PBAC Outcome

7.1 The PBAC did not recommend the General Schedule, Authority Required (Telephone/Online) listing of nemolizumab (NEMO) for the treatment of patients with severe atopic dermatitis (AD) affecting the whole body, face, and/or hands. The PBAC considered the submission's clinical claim of non-inferior effectiveness of NEMO to dupilumab (DUPI) was not adequately supported with the primary indirect comparison presented at 16 weeks indicating NEMO is likely inferior to DUPI. The Committee noted the additional clinical data on improved patient outcomes with an extended induction period out to 24 weeks presented in the PSCR, but considered this dosing regimen is not consistent with the TGA Product Information (PI), and as such cannot be considered as part of the PBS listing.

7.2 The primary reason for this outcome was due to the comparative clinical evidence.

7.3 The PBAC noted the sponsor hearing and the inputs received from the Australasian College of Dermatologists (ACD), Eczema Support Australia and a joint submission between Allergy & Anaphylaxis Australia, Australasian Society of Clinical Immunology and Allergy (ASCIA) and the National Allergy Council, were all in support of listing NEMO on the PBS for AD. The PBAC acknowledged that although the current treatments for AD have had significant benefits for patients, there is still a need to have alternative treatments available on the PBS, especially those with different mechanisms of action.

7.4 The PBAC considered the submission's nominated main comparator, DUPI, was appropriate as it is the most utilised targeted therapy for treating severe AD in clinical practice and is the therapy most likely to be replaced by NEMO should it be listed.

7.5 The PBAC noted the submission was supported by four NEMO trials (ARCADIA 1/2, ARCADIA CYLO and Study 114322) and three DUPI trials (CAFE, CHRONOS and JADE COMPARE), which were all randomised controlled trials with a low risk of bias (Table 3). The PBAC noted that the primary efficacy and safety evidence presented in the submission were indirect treatment comparisons (ITCs) of NEMO and DUPI, using the Bucher methodology via placebo. The PBAC noted the submission described NEMO as non-inferior in terms of effectiveness compared with DUPI. The PBAC noted for the ITCs presented comparing NEMO and DUPI at 16 weeks in patients with moderate and severe disease, the results were in favour of DUPI for the co-primary endpoints of EASI-75 (RR = 0.61; 95% CI: 0.41, 0.89) and IGA success (RR = 0.49; 95% CI: 0.34, 0.69). Additionally, the PBAC noted the submission did not present ITCs of NEMO versus DUPI in the proposed target population of patients with severe AD. Instead, the submission provided post-hoc subgroup analyses for patients with severe AD from the NEMO trials only.

7.6 The PBAC noted the PSCR presented additional analyses of the long-term extension phases of ARCADIA 1/2 to support an extended induction period to allow patients an additional 8 weeks of four weekly (Q4W) treatment if they have not responded at Week 16 with NEMO treatment. The PBAC noted the results presented for the ITT population indicated an additional 30.1% of patients had a positive EASI-75 response, and 9.6% more had a positive IGA response after 8 weeks additional Q4W NEMO (i.e. after 24 weeks induction). The PBAC noted the information presented, whilst presented in PSCR and not independently evaluated, indicated that some additional patients will likely achieve an adequate response with a longer Q4W induction period out to 24 weeks. However, the Committee agreed with the ESC that that the results provided limited additional support to the submission's claim of non-inferior effectiveness versus DUPI because of underlying uncertainties in the comparisons arising from it being indirect and post-hoc. The PBAC recalled it had previously noted that, in general, clinical practice with biologicals is moving towards a more extended induction period for assessment of response (paragraph 3.3, lebrikizumab PSD, March 2024 PBAC meeting), however the proposed extended induction dosing regimen for NEMO is not included in the draft TGA PI for AD. Overall, the PBAC considered NEMO was likely to be of inferior comparative effectiveness to DUPI, based on 16 weeks' treatment for both therapies, and the additional NEMO data out to 24 weeks had not been evaluated and was not supported by the PI.

7.7 The PBAC noted the submission described NEMO as non-inferior in terms of safety compared to DUPI. The PBAC agreed with the ESC that the therapeutic conclusion of non-inferior safety was uncertain. The PBAC noted that although the ITC showed similar safety of NEMO and DUPI in terms of TEAEs, the ITCs for serious TEAEs and TEAEs leading to discontinuation were statistically underpowered, indicated by the

wide 95% confidence intervals of the indirect results. In addition, the PBAC noted the selected safety outcomes in the ITCs, namely any TEAEs, serious TEAEs, TEAEs leading to discontinuation, may not allow for a meaningful comparison of NEMO and DUPI as they do not capture individual AEs that may be important.

7.8 The PBAC noted the submission presented a cost minimisation approach (CMA) for NEMO and DUPI based on the claims of non-inferior comparative effectiveness and safety. However, given its view that these claims were not supported, the PBAC considered a CMA was not an appropriate approach to the economic evaluation of NEMO and DUPI. The Committee considered an economic evaluation approach that considered the likely inferiority of NEMO to DUPI was more appropriate, however given the approach taken in the submission, cost effectiveness was unable to be assessed.

7.9 The PBAC considered the uptake rates applied to the financial estimates in the submission were uncertain and likely overestimated, given the evidence suggests that NEMO is inferior compared to DUPI in terms of effectiveness. Overall, the PBAC considered the estimated savings to the PBS/RPBS associated with the listing of NEMO are likely overestimated and unlikely to be realised.

7.10 The PBAC considered there may be two possible approaches to any resubmission, which should take the form of a standard re-entry submission:

- A re-submission based on a claim of inferior comparative effectiveness of NEMO to DUPI and include an appropriate economic evaluation that results in a lower price for NEMO commensurate with the reduced level of benefit; or
- A re-submission based on some patients accessing an extended induction period out to 24 weeks for NEMO with additional clinical comparisons and economic evaluation based on that information. The PBAC advised that any re-submission based on this approach would require both:
    - the TGA to approve the optional 24-week induction period and
    - to address the uncertainties in the comparative clinical evidence discussed in the preceding paragraphs.

7.11 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

Appendix A: Proposed Restrictions

Suggested additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough.

Initial

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
NEMOLIZUMAB					
~~nemolizumab 30 mg/0.49 mL injection, 1 x 0.49 mL pen device~~ *Nemolizumab 30 mg injection [1 chamber] (&) inert substance diluent [1 chamber], 1 dual chamber pen device*	NEW	2	2	2	Nemluvio

Concept ID	
	Category / Program: ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (telephone/electronic)
	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: Special Pricing Arrangements apply.
	Administrative Advice: The Eczema Area and Severity Index (EASI) referenced in this restriction is that described in the following literature publications: Chalmers JR et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *British Journal of Dermatology* 2014 December;171(6):1318-25. Schmitt J et al. HOME initiative collaborators. The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. *The Journal of Allergy and Clinical Immunology* 2014 October;134(4):800-7
	Administrative Advice: Instructions on the use of the Dermatology Life Quality Index and copyright details can be found here:~~,~~ https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index
	Administrative Advice: The Physician's Global Assessment (5-point scale) referenced in this restriction is that described in the following literature publication: Fatumura M et al. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: Many options, no standards Journal of the American Academy of Dermatology 2016; 674(2): 288-94 The overall appearance of dermatitis lesions is rated as 4 (severe) if the lesions are best described as featuring: deep/dark red erythema, with marked and extensive induration/papulation; excoriation and oozing/crusting are present.
	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.

	Restriction Summary [new1] / Treatment of Concept: [new1A]
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Initial treatment of the whole body
	Clinical criteria:
	Patient must have a Physicians Global Assessment (PGA) (5-point scale) baseline score of at least 4 as evidence of severe disease despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days
	AND
	Clinical criteria:
	Patient must have an Eczema Area and Severity Index (EASI) baseline score of at least 20 despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days
	AND
	Clinical criteria:
	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
	AND
	Clinical criteria:
	The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands
	AND
	Clinical criteria:
	Patient must not have experienced an inadequate response to this biological medicine in this PBS indication
	AND
	~~**Treatment**~~ ***Clinical*** **criteria:**
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	~~**AND**~~
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	~~**AND**~~
	Population criteria:
	Patient must be 12 years of age or older
	Prescribing Instructions: State each of the qualifying (i) PGA, (ii) EASI and (iii) DLQI scores in the authority application. 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. The EASI 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 in the patient's medical records.

	Restriction Summary [new3] / Treatment of Concept: [new3A]
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Initial treatment of the face and/or hands
	Clinical criteria:
	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 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
	AND
	Clinical criteria:
	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
	AND
	Clinical criteria:
	The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	AND
	Clinical criteria:
	Patient must not have experienced an inadequate response to this biological medicine in this PBS indication
	~~**AND**~~
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	~~**AND**~~
	Population criteria:
	Patient must be 12 years of age or older

3	**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.

Grandfather

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
NEMOLIZUMAB					
~~nemolizumab 30 mg/0.49 mL injection, 1 x 0.49 mL pen device~~ *Nemolizumab 30 mg injection [1 chamber] (&) inert substance diluent [1 chamber], 1 dual chamber pen device*	NEW	1	1	~~2~~3	Nemluvio

Concept ID	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (telephone/electronic)
	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: Special Pricing Arrangements apply.
	Administrative Advice: The Eczema Area and Severity Index (EASI) referenced in this restriction is that described in the following literature publications: Chalmers JR et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *British Journal of Dermatology* 2014 December;171(6):1318-25. Schmitt J et al. HOME initiative collaborators. The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. *The Journal of Allergy and Clinical Immunology* 2014 October;134(4):800-7
	Administrative Advice:

	Instructions on the use of the Dermatology Life Quality Index and copyright details can be found here:~~,~~ https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index
	Administrative Advice: The Physician's Global Assessment (5-point scale) referenced in this restriction is that described in the following literature publication: Fatumura M et al. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: Many options, no standards Journal of the American Academy of Dermatology 2016; 674(2): 288-94 The overall appearance of dermatitis lesions is rated as 4 (severe) if the lesions are best described as featuring: deep/dark red erythema, with marked and extensive induration/papulation; excoriation and oozing/crusting are present.
	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.
	Restriction Summary [new3] / Treatment of Concept: [new3A]
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply *(treatment of the whole body) – 'Grandfather' arrangements* ~~Initial treatment of the whole body~~
	Clinical criteria:
	~~Patient must have received non-PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the whole body prior to <<insert listing date>>~~ *Patient must have been receiving non-PBS-subsidised treatment with this drug for this condition prior to [date of listing]*
	AND
	Clinical criteria:
	Patient must have *had* an Eczema Area and Severity Index (EASI) baseline score of at least 20 despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days prior to commencing non-PBS-subsidised therapy with this biological medicine
	AND
	Clinical criteria:
	Patient must have had a Physicians Global Assessment (PGA) (~~5-point scale)~~ baseline score of at least 4 as evidence of severe disease despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days prior to commencing non-PBS-subsidised therapy with this biological medicine
	AND
	Clinical criteria:
	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, prior to *having commenced* ~~commencing~~ non-PBS-subsidised therapy with this biological medicine; or
	Patient must have, where the above baseline DLQI was not recorded in the patient's medical records, a current age-appropriate DLQI score (of any value) measured
	AND
	Clinical criteria:
	The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands, prior to commencing non-PBS-subsidised therapy with this biological medicine
	AND
	Clinical criteria:

	Patient must not be experiencing an inadequate response to current non-PBS-subsidised therapy with this biological medicine*, if they have received at least 16 weeks of therapy.*
	AND
	~~**Treatment**~~ ***Clinical*** **criteria:**
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	~~**AND**~~
	Population criteria:
	Patient must be 12 years of age or older
	Prescribing Instructions: *State each of the qualifying PGA, EASI and DLQI scores in the authority application. The name/s of the medium to high potency topical corticosteroids trialled prior to commencing treatment with this biological medicine must be documented in the patient's medical records.* *The EASI 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.*
	Prescribing Instructions: ~~A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.~~ *A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.*
	Prescribing Instructions: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
	Restriction Summary [new4] / Treatment of Concept: [new4A]
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - (treatment of the face and/or hands) – *'Grandfather' arrangements*
	Clinical criteria:
	~~Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the face/hands~~ *Patient must have been receiving non-PBS-subsidised treatment with this drug for this condition prior to [date of listing]*
	AND
	Clinical criteria:
	The condition must have had 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, prior to commencing non-PBS-subsidised therapy with this biological medicine; or
	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, prior to commencing non-PBS-subsidised therapy with this biological medicine
	AND
	Clinical criteria:

	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, prior to commencing non-PBS-subsidised therapy with this biological medicine; or
	Patient must have, where the above baseline DLQI was not recorded in the patient's medical records, a current age-appropriate DLQI score (of any value) measured
	AND
	Clinical criteria:
	The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands*, prior to commencing non-PBS-subsidised therapy with this biological medicine*
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	AND
	Clinical criteria:
	Patient must not be experiencing an inadequate response to current non-PBS-subsidised therapy with this biological medicine*, if they have received at least 16 weeks of therapy.*
	~~**AND**~~
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	~~**AND**~~
	Population criteria:
	~~Patient must be 12 years of age or older~~ *Patient must be at least 12 years of age.*
	Prescribing Instructions: *State each of the 4 Eczema Area and Severity Index (EASI) symptom sub-score ratings for erythema, oedema/papulation, excoriation, lichenification that were present prior to having commenced non-PBS-subsidised therapy, in the authority application. The name/s of the medium to high potency topical corticosteroids trialled prior to commencing treatment with this biological medicine is/are to be documented in the patient's medical records.* *Alternatively, state the percentage of 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.*
	Prescribing Instructions: ~~A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only.~~ ~~For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.~~ *A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.*
25398	**Prescribing Instructions:** This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.

Continuing

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
NEMOLIZUMAB					
~~nemolizumab 30 mg/0.49 mL injection, 1 x 0.49 mL pen device~~ *Nemolizumab 30 mg injection [1 chamber] (&) inert substance diluent [1 chamber], 1 dual chamber pen device*	NEW	1	1	2	Nemluvio

Concept ID	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Benefit type: ☒ Authority Required (telephone/electronic)
	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: Special Pricing Arrangements apply.
	Administrative Advice: The Eczema Area and Severity Index (EASI) referenced in this restriction is that described in the following literature publications: Chalmers JR et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *British Journal of Dermatology* 2014 December;171(6):1318-25. Schmitt J et al. HOME initiative collaborators. The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. *The Journal of Allergy and Clinical Immunology* 2014 October;134(4):800-7
	Administrative Advice: Instructions on the use of the Dermatology Life Quality Index and copyright details can be found here:~~,~~ https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index
	Administrative Advice: The Physician's Global Assessment (5-point scale) referenced in this restriction is that described in the following literature publication: Fatumura M et al. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: Many options, no standards Journal of the American Academy of Dermatology 2016; 674(2): 288-94 The overall appearance of dermatitis lesions is rated as 4 (severe) if the lesions are best described as featuring: deep/dark red erythema, with marked and extensive induration/papulation; excoriation and oozing/crusting are present.
	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.
	Restriction Summary [new5] / Treatment of Concept: [new5A]
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Continuing or resuming treatment of the whole body
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the whole body

	AND
	Clinical criteria:
	~~Patient must have achieved an adequate response prior to this first continuing treatment authority application; or~~ *Patient must have achieved an adequate response within the first 16 weeks of treatment; or*
	Patient must have maintained an adequate response to their most recent course of PBS-subsidised treatment with this biological medicine for this PBS indication if this is the second or subsequent Continuing treatment authority application; or
	Patient must have temporarily ceased treatment for reasons other than lack of response (e.g. family planning, vaccination with live vaccines, adverse-effect investigation), thereby being unable to achieve/maintain an adequate response immediately prior to this authority application
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	~~**AND**~~
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	Prescribing Instructions: For the purposes of this restriction, an adequate response to treatment of the whole body is defined as: (a) An improvement/maintenance in the Eczema Area and Severity Index (EASI) score of at least 50% compared to baseline; and (b) An improvement/maintenance in Dermatology Life Quality Index (DLQI) score of at least 4 points compared to baseline, *Where an initial baseline (post-topical corticosteroid, pre-biological medicine) DLQI score was not measured for a patient who had commenced treatment through a clinical trial, early access program or through private, non-PBS-subsidised supply, an absence of worsening in the current DLQI score compared to that measured at the time of the 'Grandfather listing' authority application will suffice as an adequate response for requirement (b) above.* State each of the current EASI and DLQI scores for this authority application.
	Restriction Summary [new6] / Treatment of Concept: [new6A]
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Continuing or resuming treatment of the face and/or hands
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the face/hands
	AND
	Clinical criteria:
	~~Patient must have achieved an adequate response prior to this first continuing treatment authority application; or~~ *Patient must have achieved an adequate response within the first 16 weeks of treatment; or*
	Patient must have maintained an adequate response to their most recent course of PBS-subsidised treatment with this biological medicine for this PBS indication if this is the second or subsequent Continuing treatment authority application; or
	Patient must have temporarily ceased treatment for reasons other than lack of response (e.g. family planning, vaccination with live vaccines, adverse-effect investigation), thereby being unable to achieve/maintain an adequate response immediately prior to this authority application

	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
	~~**AND**~~
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	Prescribing Instructions: For the purposes of this restriction, an adequate response to treatment of the face/hands is defined as: (a) (i) A rating of either mild (1) to none (0) on at least 3 of the assessments of erythema, oedema/papulation, excoriation and lichenification mentioned in the Eczema Area and Severity Index (EASI); or (ii) At least a 75% reduction in the skin area affected by this condition compared to baseline; and (b) An improvement in Dermatology Life Quality Index (DLQI) score of at least 4 points compared to baseline. *Where an initial baseline (post-topical corticosteroid, pre-biological medicine) DLQI score was not measured for a patient who had commenced treatment through a clinical trial, early access program or through private, non-PBS-subsidised supply, an absence of worsening in the current DLQI score compared to that measured at the time of the 'Grandfather listing' authority application will suffice as an adequate response for requirement (b) above.* State the current EASI ratings or the percentage of face/hand surface area affected by the condition. Also state the *current* DLQI score for this authority application.

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

8 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.

9 Sponsor's Comment

The sponsor had no comment.