

**5.01 ABROCITINIB,
Tablet 50 mg
Tablet 100 mg
Tablet 200 mg,
Cibinqo[®],
Pfizer Australia Pty Ltd**

1 Purpose of submission

- 1.1 The Category 2 submission requested a General Schedule Authority Required (Telephone/Online) listing for the treatment of adult patients with chronic severe atopic dermatitis (AD). Abrocitinib (ABRO) was requested for listing for patients who are unable to achieve disease control with daily use of topical treatments for at least 28 days.
- 1.2 Listing was requested on the basis of a cost-minimisation approach (CMA) for ABRO 200 mg once daily (QD) versus dupilumab (DUPI) 300 mg every 2 weeks (Q2W) and a cost-effectiveness analysis for ABRO 100 mg QD versus DUPI 300 mg Q2W.

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

Component	Description
Population	Adults with chronic severe AD who are candidates for systemic therapy
Intervention	ABRO 200 mg, 100 mg or 50 mg orally, QD.
Comparator	Primary: DUPI 600 mg by SC injection loading dose, followed by 300 mg by SC injection Q2W. Secondary: UPA 30 mg or 15mg orally QD.
Outcomes	EASI50+DLQI \geq 4, IGA, EASI75, EASI90, PP-NRS4, safety
Clinical claim	ABRO 200 mg: non-inferior efficacy and non-inferior safety to DUPI ABRO 100 mg: not non-inferior efficacy and non-inferior safety to DUPI

Source: Table 1.1.1, p2 of the submission.

ABRO = abrocitinib; DLQI = Dermatology Life Quality Index; DLQI \geq 4 = Proportion of patients with improvement in baseline DLQI of \geq 4 points from baseline; DUPI = DUPI; EASI50 = Proportion of patients with improvement of \geq 50% from baseline in Eczema Area and Severity Index; EASI75 = Proportion of patients with improvement of \geq 75% from baseline in Eczema Area and Severity Index; EASI90 = Proportion of patients with improvement of \geq 90% from baseline in Eczema Area and Severity Index; IGA = Investigator's Global Assessment; PP-NRS4 = Proportion of patients with \geq 4 points improvement from baseline in PP-NRS; Q2W = Once every 2 weeks; QD = Once Daily; SC = Subcutaneous; UPA = upadacitinib

2 Background

Registration status

- 2.1 ABRO is TGA approved for the following indication:

Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adults who are candidates for systemic therapy. Cibinqo can be used with or without medicated topical therapies for atopic dermatitis.

- 2.2 ABRO is available as 200 mg, 100 mg and 50 mg tablets. The Product Information (PI) states the tablets should not be split or crushed. The recommended starting dose is 100 mg or 200 mg orally QD based on individual patient characteristics. The starting dose of 100 mg QD is recommended for patients aged 65 years or more, or for patients at higher risk of venous thromboembolism (VTE), major adverse cardiovascular event (MACE) and malignancy. A dose of ABRO 200 mg QD may be appropriate for patients with high disease burden who are not at higher risk of VTE, MACE and malignancy or for patients with an inadequate response to ABRO 100 mg QD. Upon disease control, the dose should be decreased to ABRO 100 mg QD. If disease control is not maintained after a dose reduction to ABRO 100 mg QD, re-treatment with ABRO 200 mg QD can be considered. The lowest effective dose should be considered for maintenance treatment and treatment discontinuation should be considered in patients who show no evidence of therapeutic benefit after 24 weeks.
- 2.3 ABRO 50 mg QD is the recommended dose for patients taking strong inhibitors of cytochrome P450 (CYP) 2C19 and/or patients with moderate or severe renal impairment.

Previous PBAC consideration

- 2.4 A PBAC submission was previously submitted for ABRO, which was to be considered at the November 2021 PBAC meeting. Because a positive TGA Delegate’s Overview was not received prior to PBAC consideration of the submission, it was determined that ABRO should be considered at a later meeting. Following completion of the TGA review and approval, together with advice from the Department in early 2024, the original submission that had been submitted was considered outdated and was withdrawn. A new submission was presented.

3 Requested listing

- 3.1 The requested listing is presented below.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Abrocitinib – Initial treatment					
Abrocitinib 200 mg tablet	\$1,416.19 published price \$█ effective price	1	28	3	Cibinqo
Abrocitinib 100 mg tablet	\$1,416.19 published price \$█ effective price	1	28	3	Cibinqo
Abrocitinib 50 mg tablet	\$1,416.19 published price \$█ effective price	1	28	3	Cibinqo
Abrocitinib – Continuing treatment					
Abrocitinib 200 mg tablet	\$1,416.19 published price \$█ effective price	1	28	5	Cibinqo
Abrocitinib 100 mg tablet	\$1,416.19 published price \$█ effective price	1	28	5	Cibinqo
Abrocitinib 50 mg tablet	\$1,416.19 published price \$█ effective price	1	28	5	Cibinqo

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Abrocitinib – Dose change					
Abrocitinib 200 mg tablet	\$1,416.19 published price \$ [REDACTED] effective price	1	28	3	Cibinqo
Abrocitinib 100 mg tablet	\$1,416.19 published price \$ [REDACTED] effective price	1	28	3	Cibinqo
Abrocitinib 50 mg tablet	\$1,416.19 published price \$ [REDACTED] effective price	1	28	3	Cibinqo
Abrocitinib – Grandfathering					
Abrocitinib 200 mg tablet	\$1,416.19 published price \$ [REDACTED] effective price	1	28	3	Cibinqo
Abrocitinib 100 mg tablet	\$1,416.19 published price \$ [REDACTED] effective price	1	28	3	Cibinqo
Abrocitinib 50 mg tablet	\$1,416.19 published price \$ [REDACTED] effective price	1	28	3	Cibinqo

Category / Program: General Schedule
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
Episodicity: Chronic
Severity: Severe
Condition: Atopic dermatitis
Indication: Chronic severe atopic dermatitis
Treatment Phase: Initial treatment of the whole body
Clinical criteria:
<p>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 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 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 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 Patient must not have experienced an inadequate response to this therapy</p>
Treatment criteria:
<p>Must be treated by a dermatologist; OR Must be treated by a clinical immunologist; AND Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).</p>
Population criteria:
Patient must be aged 18 years or older.
Treatment Phase: Continuing treatment of whole body
Clinical criteria:

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<p>Patient must have received PBS-subsidised treatment with this therapy for the treatment of chronic severe atopic dermatitis affecting the whole body, AND Patient must have achieved an adequate response prior to this first continuing treatment authority application; OR Patient must have maintained an adequate response to their most recent supply of this therapy for this PBS indication if this is any Continuing treatment authority application other than the first; 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.</p>
<p>Treatment criteria:</p>
<p>Must be treated by a dermatologist; OR Must be treated by a clinical immunologist; AND Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).</p> <p>For the purposes of this restriction, an adequate response to treatment 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</p> <p>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.</p>
<p>Population criteria:</p>
<p>Patient must be aged 18 years or older.</p>
<p>Treatment Phase: Grandfathering - treatment of the whole body</p>
<p>Clinical criteria:</p>
<p>Patient must have been receiving non-PBS-subsidised treatment with this medicine for the treatment of chronic severe atopic dermatitis affecting the whole body; AND Prior to commencing treatment with this drug for this condition:</p> <ul style="list-style-type: none">• 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, <p>AND</p> <ul style="list-style-type: none">• 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, <p>AND 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,</p>
<p>Treatment criteria:</p>
<p>Must be treated by a dermatologist; OR Must be treated by a clinical immunologist.</p>
<p>Population criteria:</p>
<p>Patient must be aged 18 years or older.</p>

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Treatment Phase: Initial treatment of face and/or hands
Clinical criteria:
<p>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;</p> <p>OR</p> <p>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,</p> <p>AND</p> <p>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,</p> <p>AND</p> <p>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,</p> <p>AND</p> <p>Patient must not have experienced an inadequate response to this therapy.</p>
Treatment criteria:
<p>Must be treated by a dermatologist; OR</p> <p>Must be treated by a clinical immunologist;</p> <p>AND</p> <p>Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).</p>
Population criteria:
<p>Patient must be aged 18 years or older.</p>
Treatment Phase: Continuing treatment of face and/or hands
Clinical criteria:
<p>Patient must have received PBS-subsidised treatment with this therapy for the treatment of chronic severe atopic dermatitis affecting the face/hands,</p> <p>AND</p> <p>Patient must have achieved an adequate response prior to this first continuing treatment authority application;</p> <p>OR</p> <p>Patient must have maintained an adequate response to their most recent supply of this therapy for this PBS indication if this is any Continuing treatment authority application other than the first;</p> <p>OR</p> <p>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.</p>
Treatment criteria:
<p>Must be treated by a dermatologist; OR</p> <p>Must be treated by a clinical immunologist;</p> <p>AND</p> <p>Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).</p> <p>For the purposes of this restriction, an adequate response to treatment of the face/hands is defined as:</p> <p>(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</p> <p>(b) An improvement in Dermatology Life Quality Index (DLQI) score of at least 4 points compared to baseline</p>

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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.
Population criteria:
Patient must be aged 18 years or older.
Treatment Phase: Grandfathering - treatment of the face and/or hands
Clinical criteria:
Patient must have been receiving non-PBS-subsidised treatment with this medicine for the treatment of chronic severe atopic dermatitis affecting the face/hands, AND Prior to commencing treatment with this drug for this condition: <ul style="list-style-type: none"> 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; 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 <ul style="list-style-type: none"> Patient must have had 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,
Treatment criteria:
Must be treated by a dermatologist; OR Must be treated by a clinical immunologist.
Population criteria:
Patient must be aged 18 years or older.

Treatment Phase: Dose change - whole body, or face and/or hands
Treatment criteria:
Patient must not be undergoing each of: (i) commencing treatment through this treatment phase listing, (ii) treatment accessed through this treatment phase on more than 2 consecutive occasions, AND Patient must be undergoing existing PBS-subsidised treatment with this therapy where each of the following is true: (i) there is a change in daily dose, (ii) any remaining PBS repeat prescriptions for the strength that the patient is changing from, is marked as 'cancelled', AND Must be treated by a dermatologist; OR Must be treated by a clinical immunologist, AND Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).
Population criteria:
Patient must be aged 18 years or older.

Source: Table 1.4.1, p14 and the table presented on pp15-19 of the submission

3.2 A Special Pricing Arrangement (SPA) was requested for ABRO, 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. Should ABRO receive a positive recommendation from the PBAC, the sponsor stated that they are willing to work with the Department to calculate the

effective price for ABRO on a cost-minimisation basis at the agreed equi-effective doses. The ESC noted that the submission proposed flat pricing for the 100 mg and 50 mg doses, which the ESC considered may not be reasonable. The ESC also noted that the proposed price for the 100 mg dose of ABRO based on the CUA is $\frac{1}{2}$ % of the DPMQ for the 200 mg dose. The ESC advised that the PBAC may wish to consider whether pricing for the 50 mg and 100 mg doses based on a cost per mg may be more appropriate.

- 3.3 ABRO 200 mg, 100 mg and 50 mg tablets are provided in packs of 28, providing sufficient supply for 28 days (4 weeks) of treatment at the recommended dose of one tablet per day. For initial treatment, the submission proposed a maximum quantity of 1 pack with 3 repeats, which covers a 16-week initial treatment period to assess whether the patient achieves the required treatment response criteria that would permit continuing ABRO treatment, consistent with the economic analysis. If treatment response is assessed as being adequate by 16 weeks, 1 original script plus 5 repeats for continuing treatment will cover a further 24 weeks of treatment.
- 3.4 There were no criteria in the PBS restrictions requiring dose tapering during continuing treatment following an adequate treatment response. The submission proposed a separate restriction for patients who need to move between higher and lower ABRO doses to manage disease flares and to maintain the lowest effective dose.
- 3.5 As noted above, the 50 mg ABRO dose is intended for patients taking strong inhibitors of CYP 2C19 and/or patients with moderate or severe renal impairment, however the restrictions do not limit treatment these patients. The PBAC considered it was unclear whether there are likely to be patients treated with ABRO who meet these criteria.
- 3.6 A separate PBS restriction was requested for grandfathering patients involved in an ABRO Product Familiarisation Program (PFP) onto PBS reimbursed ABRO treatment. The Pre-Sub-Committee Response (PSCR) stated that up to 100 patients were anticipated for the PFP.
- 3.7 The submission requested the listing of ABRO for the treatment of adults aged ≥ 18 years with severe AD affecting the whole body, or the face and/or hands. The clinical criteria proposed in the initial and continuing listings for ABRO, in terms of disease severity and treatment response, were consistent with those for DUPI and UPA. The DUPI listing for continuing treatment specifies that the treatment response is to be assessed within the first 16 weeks of treatment. Such a restriction was not included in the proposed ABRO listing although limiting the number of repeats for initial treatment to three effectively requires patients to meet the continuing treatment criteria (which includes assessment of response) by week 16. The UPA restriction does not specify the time point for assessment of treatment response during the first 20-week treatment period covered by the initial treatment listing.
- 3.8 Under the proposed listing, patients who fail to respond to treatment with ABRO would be eligible for DUPI or UPA and vice versa; therefore, sequential use of these AD treatments would be permitted under the proposed listing. The most appropriate

sequence for their use has not been determined. The ESC noted that the American Academy of Dermatology (Davis et al, 2024) recommends DUPI as a first-line treatment, but noted that this suggestion was based on the approved indications for JAK inhibitors (including ABRO) overseas and not on actual trial data. The ESC noted the TGA approval for ABRO does not specify that patients need to have trialled DUPI first, and therefore considered it reasonable that if recommended, ABRO should be available as a first-line option along with DUPI and UPA and the proposed place of ABRO as an alternative to DUPI was reasonable. The ESC considered it would be reasonable to have a range of treatments available given the adverse event profiles differ.

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

4 Population and disease

- 4.1 AD is a chronic inflammatory disease characterised by dry skin, itching and extensive skin lesions. Symptoms may be continuous or of a relapsing-remitting nature. Patients with severe AD have more frequent symptom flaring, and their disease is characterised by skin with pronounced dryness, red lesions, papulation, crusting and skin thickening. Patients can suffer from itchy painful skin, bleeding, sleep deprivation, an increased risk of skin infections, depression, anxiety and/or suicidal intentions.
- 4.2 ABRO is a selective JAK1 inhibitor. The JAK family of enzymes (JAK1, JAK2, JAK3, and tyrosine kinase 2 [TYK2]) are associated with key cytokines/interleukins (IL) including IL-13, IL-4, IL-31, and IL-22 that have an important role in AD pathogenesis. Selective inhibition of JAK1 controls inflammatory responses involved in AD while reducing off target effects on non-inflammatory pathways mediated by other JAK enzymes.
- 4.3 The requested listing would place ABRO as an alternative to oral treatment with UPA or subcutaneous (SC) injections of DUPI or lebrikizumab (LEB) for adults with severe AD who have failed to achieve an adequate response to daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor) for at least 28 days. Long-term use of conventional oral therapies such as cyclosporine (CsA) are limited by poor tolerability and safety.
- 4.4 The proposed management algorithm in the submission states that patients may trial all PBS listed advanced treatments for chronic severe AD. Current clinical practice for use of systemic treatments for severe AD in Australia is based on a patient's prior treatments, AD disease burden, analysis of a patient's individual risks relative to the risk benefit of each advanced systemic therapy, and clinician/patient preference.

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

5 Comparator

- 5.1 The submission nominated DUPI as the main comparator. DUPI is a biologic IL-4 inhibitor listed on the PBS for use in patients aged ≥ 12 years with severe AD affecting

the whole body or the face and/or hands. The main argument provided in support of this nomination was that DUPI currently has the majority of the market share, so it is the medicine most likely to be replaced by ABRO if PBS listed. The ESC considered that nomination of DUPI as the main comparator was appropriate. However it was unclear to what extent ABRO would actually replace DUPI in clinical practice, particularly 100 mg ABRO, which has potentially inferior efficacy compared with DUPI.

- 5.2 UPA was nominated as a supplementary comparator. UPA is a selective JAK1 inhibitor and is listed on the PBS as an orally administered systemic therapy for patients aged 12 years or older with chronic severe AD. UPA was recommended by the PBAC for severe AD between the July 2021 and November 2021 PBAC meetings on a cost-minimisation basis to DUPI. Use of UPA for AD is currently around 6-fold lower in Australia than DUPI according to data from a Drug Utilisation Sub Committee (DUSC) review of DUPI in 2023. Given that ABRO and UPA have a similar mechanism of action (i.e., both selective JAK1 inhibitors), it is possible that the uptake of ABRO may be higher in patients that would otherwise have received treatment with UPA. The ESC considered that UPA is a relevant secondary comparator for the assessment of ABRO in the proposed population.
- 5.3 The submission identified three near market comparators: baricitinib (JAK1 and JAK2 inhibitor), LEB (IL-13 inhibitor) and tralokinumab (IL-13 inhibitor). Of the three, baricitinib (BARI) and LEB are currently TGA approved for severe AD. BARI was considered by PBAC for use in adults with severe AD at the July 2021 meeting but was not recommended (para 7.1, baricitinib public summary document [PSD], July 2021 PBAC meeting). LEB was recommended by the PBAC for the treatment of severe AD at the March 2024 meeting. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost effectiveness of LEB would be acceptable if it were cost-minimised to the lowest cost alternative therapy of DUPI or UPA (para 7.1, lebrizumab PSD, March 2024 PBAC meeting). At the time of ESC consideration, LEB was not yet PBS listed.
- 5.4 In the context of the CMA 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.
- 5.5 For the requested population, the following medicines may be considered alternative therapies because they could be replaced in practice: DUPI (PBS-listed), UPA (PBS-listed), LEB (positive recommendation at the March 2024 PBAC meeting, not PBS-listed yet).

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

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (4), health care professionals (1) and organisations (2) via the Consumer Comments facility on the PBS website.

6.3 The PBAC noted the advice received from Eczema Support Australia and the Australasian College of Dermatologists. Eczema Support Australia noted that a small number of patients have reported very positive outcomes with ABRO, and that it may meet the needs of patients who have not gained adequate control through other JAK inhibitors or biologics. The Australasian College of Dermatologists supported the proposed request for ABRO, noting that ABRO provides rapid relief of itch symptoms and clearance of the skin changes in patients with moderate-severe AD. The PBAC noted that this advice was supportive of the evidence provided in the submission.

6.4 Consumers noted the impact of AD on their quality of life. One consumer reported having inadequate response to DUPI and that their condition improved after starting treatment with ABRO, in particular noting that pruritis stopped, pain when showering stopped and sleep improved.

Clinical trials

6.5 The submission was primarily based on two Phase 3, head-to-head, double-blind, randomised controlled trials (RCT) comparing ABRO to DUPI (JADE COMPARE and JADE DARE). JADE COMPARE included four treatment arms: ABRO 100 mg QD, ABRO 200 mg QD, DUPI 300 mg Q2W, and placebo. JADE DARE included two treatment arms: ABRO 200 mg QD and DUPI 300 mg Q2W. The treatment durations in JADE COMPARE and JADE DARE were 16 weeks and 26 weeks, respectively.

6.6 The submission presented supplementary evidence from two non-comparative ABRO studies, JADE REGIMEN and JADE EXTEND. JADE REGIMEN provided clinical evidence of flexible dosing with ABRO 200 mg for the treatment of disease flares following loss of treatment response. The extension study JADE EXTEND assessed efficacy and safety of ABRO 200 mg and ABRO 100 mg over a longer treatment period (92 weeks).

6.7 Details of the studies presented in the submission are provided in Table 2.

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Table 2: Trials and associated reports included in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Abrocitinib versus Dupilumab (head-to-head trials)		
JADE COMPARE (NCT03720470)	A Phase 3 Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Parallel Group, Multi-Center Study Investigating the Efficacy and Safety of PF-04965842 and Dupilumab in Comparison With Placebo in Adult Subjects on Background Topical Therapy, With Moderate to Severe Atopic Dermatitis. Final Clinical Study Report.	28 May 2020
	Bieber T, <i>et al.</i> Abrocitinib versus Placebo or Dupilumab for Atopic Dermatitis.	N Engl J Med. 2021;384(12):1101-12.
JADE DARE (NCT04345367).	A Phase 3b Randomised, Double-Blind, Double-Dummy, Active Controlled Multi-Centre Study Assessing the Efficacy and Safety of Abrocitinib Compared with Dupilumab in Adult Participants on Background Topical Therapy with Moderate to Severe Atopic Dermatitis. Final Clinical Study Report.	9 December 2021.
	Reich K, <i>et al.</i> Efficacy and safety of Abrocitinib versus Dupilumab in adults with moderate-to-severe atopic dermatitis: a randomised, double-blind, multicentre phase 3 trial.	Lancet. 2022; 400 (10348): 273-282.
Supplementary evidence (non-comparative Abrocitinib studies)		
JADE REGIMEN (NCT03627767)	A Phase 3 Randomized Withdrawal, Double-Blind, Placebo-Controlled, Multi-Center Study Investigating the Efficacy and Safety of Abrocitinib (PF-04965842) in Subjects Aged 12 Years and Over, With Moderate to Severe Atopic Dermatitis With the Option of Rescue Treatment in Flaring Subjects. Final Clinical Study Report.	8 February 2021
JADE EXTEND (NCT03422822)	Phase 3 study to evaluate Abrocitinib with or without Topical Medications in patients aged 12 years and older who have moderate to severe atopic dermatitis and have completed a qualifying parent study. Interim Clinical Study Report.	22 April 2020 (interim analysis DCO)
	Reich K, <i>et al.</i> Abrocitinib efficacy and safety in patients with moderate-to-severe atopic dermatitis: Results from phase 3 studies, including the long-term extension JADE EXTEND study.	J Eur Acad Dermatol Venereol 2023; 37(10):2056-2066.
	Correction to 'Reich. Abrocitinib efficacy and safety in patients with moderate-to-severe atopic dermatitis: Results from phase 3 studies, including the long-term extension JADE EXTEND study'	J Eur Acad Dermatol Venereol 2023; 37(12):2608-2609.

Source: Table 2.1.3, p27 of the submission.

ABRO = abrocitinib; AD = Atopic Dermatitis; DCO = Data cut-off; DUPI = dupilumab; PBAC = Pharmaceutical Benefits Advisory Committee; UPA = upadacitinib

6.8 Key features of the evidence are summarised in Table 3.

Table 3: Key features of the included evidence to support the clinical claim

Trial	N	Design/ duration	Risk of bias	Relevant comparison	Patient population	Outcome(s)
ABRO versus DUPI trials (head-to-head trials)						
JADE COMPARE	838	P3, R, MC, DB, DD, PC 16 wk, rescue therapy ^a	Low	ABRO 100 mg QD + TCS/TCI	M-S AD; adults	IGA response at Wk12 EASI75 at Wk 12 PP-NRS4 at Wk 2 EASI50+DLQI \geq 4 at Wk 16 Safety
				ABRO 200 mg QD + TCS/TCI		
				DUPI 300 mg Q2W + TCS/TCI		
				PBO + TCS/TCI		
JADE DARE	727	P3, R, MC, DB, DD, AC 26 wk, rescue therapy ^a	Low	ABRO 200 mg QD + TCS	M-S AD; adults	EASI90 at Wk 4 PP-NRS4 at Wk 2 EASI50+DLQI \geq 4 at Wk 16 Safety
				DUPI 300 mg QD + TCS		
ABRO (Supplementary evidence)						
JADE REGIMEN	1235	R, DB, MC, PC 52 wk Flare rescue treatment ^b	Low	ABRO 100 mg QD	M-S AD; adults & adolescents	IGA response after flare rescue treatment EASI75 after flare rescue treatment
				ABRO 200 mg QD		
				PBO		
JADE EXTEND	1590	R, DB, MC, AC 92 wk (Ongoing)	Low	ABRO 100 mg QD \pm TCS	M-S AD; adults & adolescents	EASI50+DLQI \geq 4 at Wk 48 (interim analysis) Safety
				ABRO 200 mg QD \pm TCS		

Source: Table 2.2.1, p29 of the submission.

ABRO = abrocitinib; AC = active control; AD = atopic dermatitis; DB = double blind; DD = double dummy; DLQI = Dermatology Life Quality Index; DLQI \geq 4 = proportion of patients with improvement in baseline DLQI of \geq 4 points from baseline; DUPI = dupilumab; EASI = Eczema Area and Severity Index; EASI 50/75/90 = proportion of patients with improvement of \geq 50%/75%/90% from baseline in EASI; IGA = Investigator's Global Assessment; IGA response = proportion of patients with IGA response of clear (0) or almost clear (1) + \geq 2 points improvement from baseline; MC = multi-centre; M-S = moderate to severe; P3 = phase 3; PBO = placebo; PC = placebo-control; PDE-4 = phosphodiesterase 4; PP-NRS = Peak Pruritus Numerical Rating Scale; PP-NRS4 = proportion of patients with \geq 4 points improvement from baseline in PP-NRS; R = randomised; TCI = topical calcineurin inhibitors; TCS = topical corticosteroids; UPA = Upadacitinib; wk = week.

^a Protocols allowed investigators to rescue patients who were experiencing unacceptable or worsening of symptoms. Patients who received rescue therapy were discontinued from study treatment and considered non-responders.

^b Rescue treatment of flare with open label ABRO 200 mg + topical therapy (TCS, TCI, PDE-4) for 12 weeks

6.9 JADE COMPARE and JADE DARE included adults aged \geq 18 years with chronic moderate to severe AD who had an inadequate response to treatment with medicated topical therapy (topical corticosteroids [TCS]/ topical calcineurin inhibitors [TCI]) for AD for at least 28 days or required systemic therapies for control of their disease.

6.10 The eligibility criteria of JADE COMPARE and JADE DARE were not aligned with the requested PBS restrictions as follows:

- Both clinical trials included patients with moderate to severe AD defined as affected body surface area (BSA) \geq 10%, Investigator's Global Assessment (IGA)¹ score \geq 3, Eczema Area and Severity Index (EASI) score \geq 16, and Pruritus Numerical Rating Scale (NRS) severity score of \geq 4 at baseline. This population was broader than the proposed PBS population of severe AD which was defined as EASI \geq 20, PGA=4 and

¹ The IGA is equivalent to the Physician's Global Assessment (PGA) tool included in the PBS listing for ABRO.

any age-appropriate Dermatology Life Quality Index (DLQI) score. Therefore, the submission relied on post hoc subgroup analyses of patients with severe AD (defined as IGA=4 only) to support the use of ABRO in the proposed PBS population. The submission stated that most participants in the trials with IGA=4 at baseline also had an EASI score ≥ 20 . Therefore, results of these analyses would not be expected to differ for a severe AD subgroup based only on the baseline IGA score. The PSCR stated that approximately 95% of JADE COMPARE patients with an IGA score of 4 across all treatment arms also had an EASI score of ≥ 20 and reiterated that the results for the subgroup analyses are applicable to the proposed PBS population.

- There were no eligibility criteria in the trials specifically relevant to disease severity of AD affecting the face and/or hands.
 - Patients who had received prior treatment with any systemic JAK inhibitors, IL-4 or IL-13 antagonists (DUPI, UPA, or LEB) were excluded from the trials but not from the requested PBS listing.
- 6.11 The co-primary endpoints in JADE COMPARE were EASI75 ($\geq 75\%$ improvement in EASI score from baseline) and IGA response (IGA of clear (0) or almost clear (1) and ≥ 2 points improvement from baseline) at Week 12. Secondary endpoints included assessment of EASI75 and IGA response at Week 16 and PP-NRS4 (≥ 4 points improvement from baseline in Peak Pruritus Numerical Rating Scale) at Week 2. The co-primary endpoints in JADE DARE were PP-NRS4 at Week 2 and EASI90 ($\geq 90\%$ improvement in EASI score from baseline) at Week 4.
- 6.12 The submission noted that the outcome preferred by PBAC for assessment of systemic treatments for severe AD affecting the whole body was a composite endpoint EASI50+DLQI ≥ 4 ($\geq 50\%$ improvement from baseline in EASI score and an improvement in DLQI from baseline of ≥ 4 points) as it is consistent with the continuing criteria in the PBS listings of systemic treatments for whole body severe AD. The ESC previously noted that using a marker of lesions (EASI) and patient impact (DLQI) for continuing criteria is broadly consistent with Australian consensus guidelines. In its consideration for DUPI in March 2020 the PBAC agreed with the ESC that the proposed approach was likely to be clinically reasonable and able to capture patients with a meaningful response to treatment (para 7.4, DUPI PSD, March 2020 PBAC meeting).
- 6.13 The composite endpoint of EASI50+DLQI ≥ 4 was not a pre-specified outcome in either of the head-to-head RCTs, JADE COMPARE or JADE DARE. However, both individual outcome measures (EASI50 and DLQI ≥ 4) were assessed in participants throughout the studies. In addition, the clinical trials included participants outside the PBS restriction (adults with moderate AD). Therefore, post hoc subgroup analyses were conducted based on the individual patient data from JADE COMPARE and JADE DARE to obtain results for the composite endpoint of EASI50+DLQI ≥ 4 for adults with severe AD. The assessment of the composite outcome EASI50+DLQI ≥ 4 in the subgroup analyses was presented at a single time point (Week 16); however, the relative effectiveness of

ABRO versus DUPI varies over time due to differences in time to the onset of treatment response and time to the plateauing of treatment response. The PSCR stated that Week 16 was chosen as the time point to assess efficacy as this is the time point in the existing PBS restrictions for DUPI. The PSCR noted that by focussing on Week 16 the submission did not quantify the benefits of ABRO over DUPI through its earlier onset of action. The ESC considered that assessment of response at 16 weeks was likely reasonable.

- 6.14 Clinical evidence supporting the proposed listing for adults with severe AD affecting the face and/or hands was scarce. The effectiveness of ABRO 200 mg, ABRO 100 mg, and DUPI 300 mg for the treatment of face AD was based on a published² post hoc analysis of change from baseline in the EASI head and neck region score at Week 16 in the intention-to-treat (ITT) population of JADE COMPARE. This outcome was not aligned with the PBS continuation criteria for the face and/or hands. Data for patients with severe AD affecting the hands were not presented in the submission. The PSCR acknowledged that the analysis wasn't perfectly aligned with the treatment response criteria, however requested this be an additional option for patients alongside DUPI and UPA, based on previous PBAC precedent for DUPI and UPA. The ESC noted that there were similar limitations with the data available for DUPI and UPA and that the submission had taken the same approach to demonstrate the effects were similar across body regions, which was reasonable.
- 6.15 The patient demographics and disease characteristics at baseline were broadly comparable across study arms within trials and between JADE COMPARE and JADE DARE. The submission did not present the baseline demographic or disease characteristics of the patients in the two severe AD subgroups (severe AD with no prior systemic treatment and severe AD with prior systemic treatment) that were used in the post hoc analyses to support the clinical claims in the proposed PBS population. Randomisation was not stratified according to disease severity in JADE COMPARE but was in JADE DARE; neither trial used prior systemic treatment as a stratification factor at randomisation. These were considered potential treatment effect modifiers in the submission.
- 6.16 Patients in JADE REGIMEN and JADE EXTEND received ABRO treatment only. Therefore, JADE REGIMEN did not provide comparative evidence for flexible dosing of ABRO versus DUPI to support the clinical claim in the submission. Similarly, the extension study JADE EXTEND did not provide comparative evidence of effectiveness or safety for ABRO versus DUPI.
- 6.17 In Appendix 4 to the main submission, supplementary anchored indirect treatment comparisons (ITCs) of ABRO versus UPA, via placebo as the common reference, were provided. ITCs were based on:

² Alexis A, de Bruin-Weller M, et al. Rapidity of Improvement in Signs/Symptoms of Moderate-to-Severe Atopic Dermatitis by Body Region with ABRO in the Phase 3 JADE COMPARE Study. *Dermatol Ther (Heidelb)*. 2022;12(3):771-85.

- 1) ABRO and placebo arms of JADE COMPARE versus UPA and placebo arms of an UPA trial (AD UP). These studies permitted concomitant use of topical emollients, and topical medicated therapies such as TCS.
- 2) ABRO monotherapy studies (JADE MONO-1 and JADE MONO-2) versus UPA monotherapy studies (MEASURE UP-1 and MEASURE UP-2).
- 3) Meta-analysis of data from the studies above (monotherapy and combination therapy) for ABRO versus UPA.

The data from the UPA trials included in ITCs were sourced from the UPA PSD, July 2021 PBAC meeting.

6.18 Limitations regarding the ITCs of ABRO with UPA were:

- The AD UP study of UPA versus placebo included adolescents aged ≥ 12 to 17 years in the study population; whereas the ABRO trials included adult patients only.
- In the ITC presented in the UPA PSD (para 6.25, UPA PSD, July 2021 PBAC meeting), AD UP participants with severe AD were defined as EASI ≥ 20 and IGA=4 at baseline; while JADE COMPARE participants with severe AD included in the ITC to UPA were assessed as having severe AD based only on IGA=4 at baseline.
- The small number of patients in the severe AD subgroups indirectly compared led to wide 95% confidence intervals (CIs) of the indirect estimates, based on which no firm non-inferiority conclusion could be made.
- The ITCs were based on post hoc analyses of an endpoint that was not prespecified in the trials.
- Data on baseline disease characteristics and demographics were not provided for the subgroups included in the ITCs.

6.19 No clinical claim for ABRO versus UPA was made in the submission. The PBAC submission for UPA relied on the results of an ITC between UPA and DUPI via placebo as a common comparator because the head-to-head trial of UPA versus DUPI (HEADS UP) did not include the 15 mg dose of UPA and did not include assessment of DLQI. The PBAC's recommendation for listing of UPA was based on, among other matters, its assessment that the cost-effectiveness of UPA would be acceptable if it were cost-minimised against DUPI. The PBAC advised that the equi-effective doses are UPA 15 mg or 30 mg QD and DUPI 600 mg as an initial dose then 300 mg Q2W thereafter, or DUPI 400 mg as an initial dose then 200 mg Q2W thereafter in adolescents with a body weight <60kg (not within the PBS target population for ABRO), assuming equivalent drug costs over a two-year period (para. 9.1, UPA PSD, July 2021 PBAC meeting).

Comparative effectiveness

ABRO vs. DUPI: adults with moderate to severe AD (ITT population)

6.20 The results of the primary and key secondary outcomes from JADE COMPARE and JADE DARE in the ITT population with moderate to severe AD are presented in Table 4.

Table 4: Results of primary and key secondary outcomes in JADE COMPARE and JADE DARE trial (ITT)

Endpoint	ABRO 100 mg QD n/N (%)	ABRO 200 mg QD n/N (%)	DUPI 300 mg Q2W n/N (%)	PBO n/N (%)	RR [95% CI]	OR [95% CI]	RD, % [95% CI]
JADE COMPARE							
IGA response Week 12	86/235 (36.6)	–	88/241 (36.5)	–	1.00 [0.79, 1.27]	1.00 [0.69, 1.46]	0.05 [-8.0, 9.1]
	–	106/219 (48.4)	88/241 (36.5)	–	1.33 [1.07, 1.64]	1.63 [1.12, 2.37]	12.4 [3.5, 21.3]
	–	–	–	18/129 (14.0)	–	–	–
EASI75 Week 12	138/235 (58.7)	–	140/241 (58.1)	–	1.01 [0.87, 1.18]	1.03 [0.71, 1.48]	0.8 [-8.1, 9.6]
	–	154/219 (70.3)	140/241 (58.1)	–	1.21 [1.06, 1.39]	1.71 [1.16, 2.52]	12.0 [2.8, 20.2]
	–	–	–	35/129 (27.1)	–	–	–
PP-NRS4 Week 2	75/236 (31.8)	–	63/239 (26.4)	–	1.21 [0.91, 1.60]	1.30 [0.87, 1.94]	5.2 [-2.9, 13.4] p=0.2084
	–	111/226 (49.1)	63/239 (26.4)	–	1.78 [1.39, 2.29]	2.48 [1.69, 3.65]	22.1 [13.5, 30.7] p<0.0001
	–	–	–	18/130 (13.8)	–	–	–
JADE DARE							
PP-NRS4 Week 2	–	172/357 (48.2)	93/364 (25.5)	–	1.89 [1.54, 2.32]	2.71 [1.98, 3.71]	22.6 [15.8, 29.5] p<0.0001
EASI90 Week 4	–	101/ (28.5)	53/364 (14.6)	–	1.96 [1.45, 2.64]	2.34 [1.62, 3.40]	14.1 [8.2, 20.0] p<0.0001

Source: Table 2.6.1, p40; Table 2.6.2, p42; Table 2.6.3 p43; and Table 2.6.4, p44 of the submission

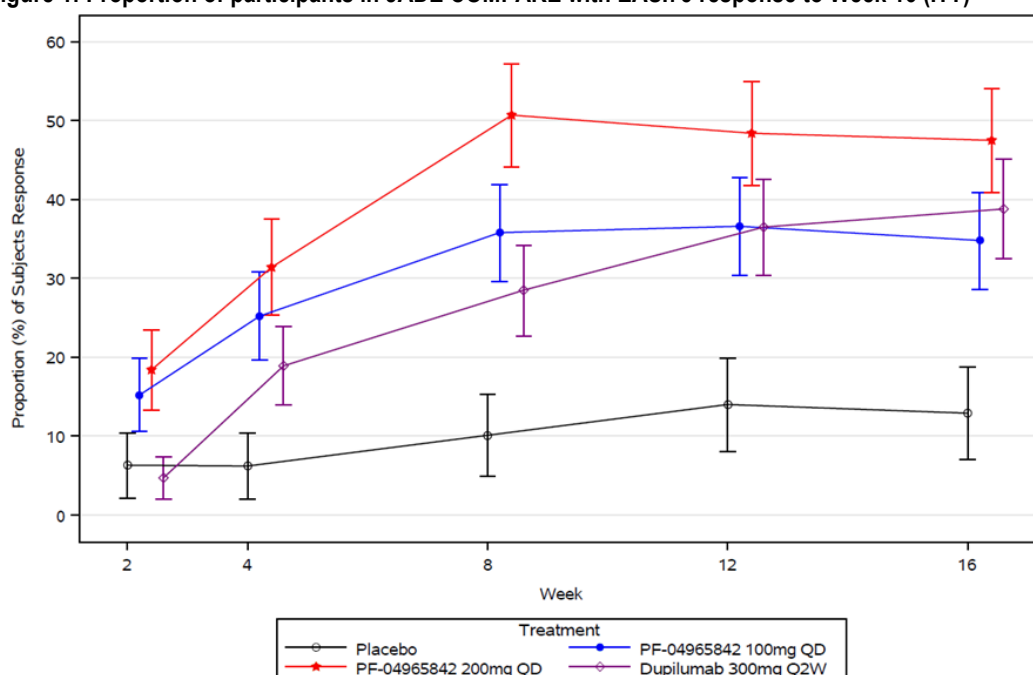
ABRO = abrocitinib; CI = Confidence Interval; DUPI = dupilumab; EASI75 = Proportion of patients with improvement of ≥ 75% from baseline in Eczema Area and Severity Index; EASI90 = Proportion of patients with improvement of ≥ 90% from baseline in Eczema Area and Severity Index; IGA = Investigator's Global Assessment; IGA response = Proportion of patients with IGA response of clear (0) or almost clear (1) + ≥2 points improvement from baseline; ITT = Intention to treat; OR = Odds ratio; PBO = Placebo; PP = per protocol; PP-NRS4 = Proportion of patients with ≥4 points improvement from baseline in PP-NRS; Q2W = Once every 2 weeks; QD = Once Daily; RD = Risk Difference; RR = Relative Risk.

Notes: Risk difference as reported in the JADE COMPARE Clinical Study Report. The estimate and 95% CI for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. 95% CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders). Relative risk and odds ratio was calculated based on the number of patients in the treatment groups in RevMan v5.0 software, using a random effects model.

Results in bold are statistically significant.

- 6.21 Results for the co-primary endpoints in JADE COMPARE suggested that ABRO 200 mg is superior to DUPI 300 mg in terms of IGA response and EASI75 at Week 12 for treatment of moderate to severe AD (IGA response: 48.4% vs. 36.5%, risk difference [RD]³: 12.4% [95% CI: 3.5, 21.3]; EASI75: 70.3% vs. 58.1%, RD: 12.0% [95% CI: 2.8, 20.2]). Similar results were reported for IGA response and EASI75 response at Week 12 in JADE DARE which were assessed as secondary endpoints. Although the comparisons were not statistically tested, the 95% CIs of the RD excluded zero.
- 6.22 Results for the co-primary endpoints at Week 12 were similar between the ABRO 100 mg QD and DUPI 300 mg Q2W arms in JADE COMPARE (IGA response: 36.6% vs. 36.5%, RD: 0.05% [95% CI: -8.0, 9.1]; EASI75: 58.7% vs. 58.1%, RD: 0.8% [95% CI: -8.1, 9.6]).
- 6.23 Both IGA response and EASI75 data were collected at Weeks 2, 4, 8, 12 and 16 in JADE COMPARE (Figure 1 and Figure 2). An earlier onset of treatment response was observed for both doses of ABRO compared to DUPI with a difference continuing up to Week 8. Response to treatment with ABRO 100 mg and 200 mg was plateauing from Week 8 onwards while response to DUPI continued to increase to Week 16.

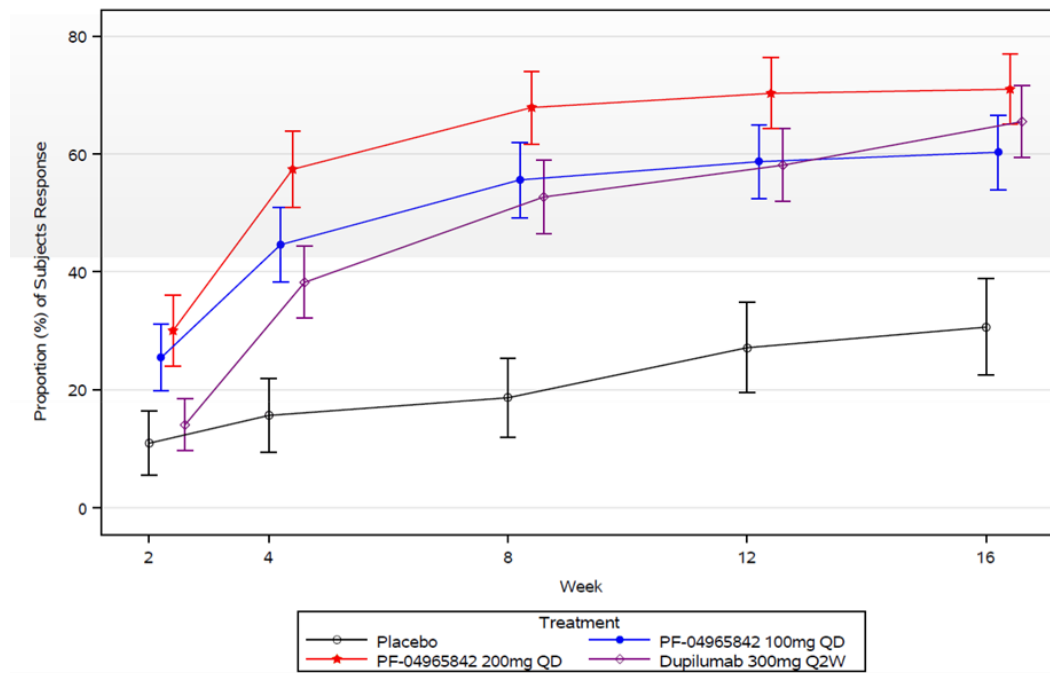
Figure 1: Proportion of participants in JADE COMPARE with EASI75 response to Week 16 (ITT)



Source: Figure 2.6.1, p41 in the submission
 ITT = intention-to-treat; QD = once daily; Q2W = once every two weeks
 Note: PF-04965842 is ABRO.

³ The estimate and 95% CI for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. 95% CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders).

Figure 2: Proportion of participants in JADE COMPARE with an IGA response to Week 16 (ITT)



Source: Figure 2.6.2, p42 in the submission
 ITT = intention-to-treat; QD = once daily; Q2W = once every two weeks
 Note: PF-04965842 refers to abrocitinib

- 6.24 IGA response and EASI75 response were assessed in JADE DARE beyond Week 16 to Week 26. At Week 26, there was no statistically significant difference between the ABRO 200 mg and DUPI 300 mg arms for IGA response (55.6% vs. 51.1%; RD: 4.5 [95% CI: -2.8, 11.8], $p=0.2293$) or EASI75 response (73.0% vs. 72.3%; RD: 0.7 [95% CI: -5.9, 7.2], $p=0.8395$). These data support observations at Week 16 that the difference in response rate between the ABRO 200 mg and DUPI 300 mg arms was decreasing over time with the curve for DUPI 300 mg plateauing from Week 20 and response to ABRO 200 mg plateauing from Week 16.
- 6.25 Onset of pruritis (itch) relief assessed as PP-NRS4 response at Week 2 was more rapid with ABRO 200 mg compared with DUPI 300 mg in JADE COMPARE. The proportion of participants achieving PP-NRS4 with ABRO 200 mg was significantly higher than DUPI 300 mg at Week 2 in both JADE COMPARE (RD: 22.1% [95% CI: 13.5, 30.7]; $p<0.0001$) and JADE DARE (RD: 22.6% [95% CI: 15.8, 29.5]; $p<0.0001$). The proportion of patients achieving PP-NRS4 at Week 2 was not statistically significantly different between ABRO 100 mg and DUPI 300 mg in JADE COMPARE (RD: 5.2% [95% CI: -2.9, 13.4]; $p=0.2084$). A similar trend to IGA and EASI75 responses was observed for PP-NRS4 response over time with the responder rate to both doses of ABRO plateauing at Week 8 but continuing to rise for DUPI to Week 16. From Week 16 to Week 26, the response rate for ABRO 200 mg was comparable to DUPI 300 mg for PP-NRS4 (Week 16: RD: 3.6 [95%CI: -3.4, 10.5], $p=0.3144$; Week 26: RD: 5.0, [95% CI: -1.9, 11.9], $p=0.1601$), with no statistically significant difference observed.

- 6.26 In JADE DARE, more patients treated with ABRO 200 mg versus DUPI 300 mg achieved a 90% improvement in their EASI score (EASI90) at Week 4 (28.5% vs. 14.6%; RD: 14.1% [95% CI: 8.2, 20.0]; $p < 0.0001$), with similar results reported from JADE COMPARE (32.3% vs. 12.2%; RD: 20.6% [95% CI: 13.2, 27.9]), further supporting an earlier onset of treatment response with ABRO 200 mg versus DUPI 300 mg. In JADE DARE, the difference in response rate for ABRO 200 mg versus DUPI 300 mg was statistically significant at all time points up to Week 20, but not at Week 26.
- 6.27 Evidence supporting the proposed PBS restriction for the face and/or hands was based on post hoc analyses of the EASI head and neck scores in adults with moderate to severe AD (ITT population) from JADE COMPARE only. Differences in the EASI head and neck scores between ABRO and DUPI arms in JADE COMPARE were presented as least square mean (LSM) change in the EASI head and neck region scores. The trends for both doses of ABRO and for DUPI observed for IGA response and EASI75 response for whole body moderate to severe AD to Week 16 in JADE COMPARE were also observed for change in the EASI head and neck region scores over the same period. Treatment with ABRO 200 mg resulted in a LSM reduction of 52.5% at Week 2 and 76.6% at Week 16 in the head and neck region EASI score from baseline.⁴ The median (95% CI) time to achieving an EASI75 score for the head and neck region was 29 days (29, 32) with ABRO 200 mg, 57 days (31, 58) with ABRO 100 mg and 57 days (56, 83) with DUPI 300 mg suggesting that the time to response was faster for ABRO 200 mg than DUPI 300 mg but comparable for ABRO 100 mg versus DUPI 300 mg.

ABRO vs. DUPI: post hoc analyses of EASI50+DLQI \geq 4

- 6.28 Results for the composite endpoint of EASI50+DLQI \geq 4 for ABRO versus DUPI in subgroups relevant to the PBS listing (severe AD with no prior systemic treatment and severe AD with prior systemic treatment) from JADE COMPARE and JADE DARE at Week 16 are presented in Table 5. The subgroups were small, leading to uncertainty in the estimates of effectiveness. Subgroup populations from JADE COMPARE and JADE DARE were pooled for the comparison of ABRO 200 mg and DUPI 300 mg for these analyses to increase the sample size.

⁴ Alexis A, et al. Rapidity of Improvement in Signs/Symptoms of Moderate-to-Severe Atopic Dermatitis by Body Region with ABRO in the Phase 3 JADE COMPARE Study. *Dermatol Ther (Heidelb)*. 2022;12(3):771-85.

Table 5: Subgroup analysis results for EASI50+DLQI≥4 response rate at Week 16

	Trial	ABRO 100 mg QD n/N (%)	ABRO 200 mg QD n/N (%)	PBO n/N (%)	DUPI 300 mg Q2W n/N (%)	ABRO vs. DUPI		
						RR [95% CI]	OR [95% CI]	RD, % [95% CI]
Severe AD IGA=4, No Prior IMM	JADE COMPARE	44/67 (65.7)	–	15/32 (46.9)	35/49 (71.4)	–	–	-5.8 [-22.8, 11.3]
		–	49/58 (84.5)	–	35/49 (71.4)	1.18 [0.96, 1.46]	2.18 [0.85, 5.59]	13.1 [-2.7, 28.8]
	JADE DARE	–	58/71 (81.7)	–	45/63 (71.4)	1.14 [0.94, 1.38]	1.78 [0.79, 4.02]	10.3 [-4.1, 24.6]
	Pooled	–	107/129 (82.9)	–	80/112 (71.4)	1.16 [1.01, 1.34]	1.94 [1.05, 3.60]	11.5 [-0.9, 22.1] ^a
Severe AD IGA=4, Prior IMM	JADE COMPARE	9/14 (64.3)	–	1/10 (10.0)	20/25 (80.0)	–	–	-15.7 [-45.3, 13.9]
		–	25/29 (86.2)	–	20/25 (80.0)	1.08 [0.84, 1.38]	1.56 [0.37, 6.60]	6.2 [-19.9, 26.3]
	JADE DARE	–	58/75 (77.3)	–	63/81 (77.8)	0.99 [0.84, 1.18]	0.97 [0.46, 2.07]	-0.4 [-13.6, 12.7]
	Pooled data	–	83/104 (79.8)	–	83/106 (78.3)	1.02 [0.89, 1.17]	1.08 [0.55, 2.10]	1.5 [-9.5, 12.5] ^a

Source: Table 2.7.1, p76 of the submission

ABRO = abrocitinib; AD = Atopic Dermatitis; CI = Confidence Interval; DLQI = Dermatology Life Quality Index; DLQI≥4 = Proportion of patients with improvement in baseline DLQI of ≥4 points from baseline; DUPI = DUPI; EASI50 = Proportion of patients with improvement of ≥ 50% from baseline in Eczema Area and Severity Index; IGA = Investigator's Global Assessment; IMM = Immunomodulatory therapy; OR = Odds ratio; PBO = Placebo; Q2W = Once every 2 weeks; QD = Once Daily; RD = Risk Difference; RR = Relative risk.

Notes: The estimate and 95% CI for difference were calculated based on the CMH-weighted average difference for each stratification factors (study, baseline disease severity and age category) using the normal approximation of binomial proportions.

Relative risk and odds ratio calculated based on the number of patients in the treatment groups in RevMan v5.0 software, using a random effects model. Risk difference as reported in analysis.

^a Data presented in the table on risk differences for pooled ABRO 200 mg versus DUPI were incorrect in the submission and were calculated during the evaluation, based on the pooled proportions.

Note that the results presented in Table 5 are derived from post-hoc analyses conducted by the applicant and during the evaluation specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plans for JADE COMPARE or JADE DARE. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

6.29 For severe AD subgroups with no prior systemic therapy, the response rates for the EASI50+DLQI≥4 endpoint at Week 16 were numerically higher for ABRO 200 mg versus DUPI 300 mg in JADE COMPARE (84.5% vs. 71.4%; RD: 13.1% [95% CI: -2.7, 28.8]), in JADE DARE (81.7% vs. 71.4%; RD: 10.3% [95% CI: -4.1, 24.6]) and in pooled populations (82.9% vs. 71.4%; RD: 11.5% [95% CI: -0.9, 22.1]). The 95% CI did not include a worsening of the outcome that may be clinically relevant. Results for the EASI50+DLQI≥4 endpoint in the ITT population (i.e., adults with moderate to severe AD) support the claim of non-inferiority for ABRO 200 mg QD versus DUPI 300 mg Q2W.

6.30 For the severe AD subgroup with no prior systemic therapy from JADE COMPARE, a numerically lower response rate for the EASI50+DLQI≥4 endpoint at Week 16 was observed for ABRO 100 mg versus DUPI 300 mg (65.7% vs. 71.4%; RD: -5.8% [95% CI: -22.8, 11.3]). The lower end of the 95% CI suggested a reduction in the responder rate of 22.8%, which is likely to be clinically relevant. Results for the EASI50+DLQI≥4 endpoint in the ITT population (i.e., adults with moderate to severe AD) support the claim of inferiority for ABRO 100 mg QD versus DUPI 300 mg Q2W, with the 95% CI including a worsening of the outcome.

- 6.31 For severe AD subgroups with prior systemic therapy, the sample size was very small and so the estimate of comparative efficacy for ABRO 100 mg QD versus DUPI 300 Q2W was highly uncertain and had a wide 95% CI. The pooled data for EASI50+DLQI≥4 at Week 16 showed comparable responder rates for ABRO 200 mg QD versus DUPI 300 mg Q2W (79.8% vs. 78.3%; RD: 1.5% [95% CI: -9.5, 12.5]).
- 6.32 Limitations of the evidence related to the post hoc nature of the analyses in small subgroups. The included studies were not designed for comparison of ABRO and DUPI for the composite outcome.

Comparative harms

- 6.33 A summary of all-cause treatment emergent adverse events (TEAEs) in the ABRO and DUPI arms of the JADE COMPARE and JADE DARE studies is presented in Table 6.

Table 6: Summary of TEAEs – all causalities (SAS)

	JADE COMPARE				JADE DARE	
	PBO (N=131)	ABRO 100 mg QD (N=238)	ABRO 200 mg QD (N=226)	DUPI 300 mg Q2W (N=242)	ABRO 200 mg QD (N=362)	DUPI 300 mg QD (N=365)
Number of adverse events, n	150	269	308	223	817	600
Subjects with adverse events, n (%)	70 (53.4)	121 (50.8)	140 (61.9)	121 (50.0)	268 (74.0)	239 (65.5)
Subjects with serious adverse events, n (%)	5 (3.8)	6 (2.5)	2 (0.9)	2 (0.8)	6 (1.7)	6 (1.6)
Subjects with severe adverse events, n (%)	3 (2.3)	5 (2.1)	4 (1.8)	2 (0.8)	11 (3.0)	8 (2.2)
Subjects discontinued from study due to adverse events ^a , n (%)	5 (3.8)	6 (2.5)	10 (4.4)	8 (3.3)	12 (3.3)	9 (2.5)
Subjects discontinued study drug due to AE and continued study ^b , n (%)	2 (1.5)	2 (0.8)	1 (0.4)	0	0	1 (0.3)
Subjects with temporary discontinuation due to adverse events, n (%)	9 (6.9)	15 (6.3)	12 (5.3)	9 (3.7)	39 (10.8)	27 (7.4)

Source: Table 2.6.13, p52 of the submission

ABRO = abrocitinib; AE = Adverse Event; DUPI = DUPI; PBO = Placebo; Q2W = Once every 2 weeks; QD = Once Daily; SAS = Safety Analysis Set; TEAE = Treatment-emergent adverse events.

Notes: Included data up to 28 days after last dose of study.

Except for the number of adverse events subjects were counted only once per treatment in each row.

MedDRA v22.1 (JADE COMPARE) and MedDRA v24.0 (JADE DARE) coding dictionary applied.

^a Subjects who had an AE record that indicated that the AE caused the subject to be discontinued from the study. Three subjects (13089008, 13469002, 12479010) had an AE that started before Week 16 and discontinued due to that AE after Week 16. Those AEs were also included in this table.

^b Subjects who had an AE record that indicated that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study

- 6.34 The number of TEAEs and the number of participants with TEAEs were higher in the ABRO 200 mg arm compared with the DUPI 300 mg arm in both studies although most TEAEs were reported as mild or moderate in severity. The proportion of participants with serious adverse events (SAEs), severe TEAEs, and TEAEs leading to study discontinuation or treatment discontinuation was low and similar across study arms.
- 6.35 No deaths were reported in JADE COMPARE during the study period. Two (0.6%) deaths occurred in the ABRO 200 mg QD arm of JADE DARE (COVID-19 infection;

cardio-respiratory arrest and intracranial haemorrhage); but neither death was considered treatment-related.

- 6.36 A summary of treatment-related TEAEs in both studies by System Organ Class and Preferred Term are presented in Table 7 and Table 8. The incidence of treatment-related TEAEs was higher in the ABRO 200 mg arm (29.6%) than in the ABRO 100 mg arm (19.7%) and the DUPI 300 mg arm (16.9%) in JADE COMPARE; the same trend was observed for ABRO 200 mg versus DUPI 300 mg in JADE DARE (34.5% vs. 15.6%). The incidence of conjunctivitis was higher in the DUPI 300 mg arm; and the incidence of nausea, acne, herpes simplex, herpes zoster and folliculitis were higher in the ABRO 200 mg arm. Overall, fewer treatment-related TEAEs were observed in the ABRO 100 mg QD versus ABRO 200 mg QD arms of JADE COMPARE, except for nasopharyngitis (3.8% vs 1.8%). The incidence of treatment-related TEAEs was similar for ABRO 100 mg versus DUPI 300 mg except for conjunctivitis, which is known to be associated with DUPI treatment.

Table 7: Summary of treatment-related TEAEs (≥2%) from JADE COMPARE

	JADE COMPARE				RR ABRO vs DUPI (95% CI)	
	PBO (N=131)	ABRO 100 mg QD (N=238)	ABRO 200 mg QD (N=226)	DUPI 300 mg Q2W (N=242)	ABRO 100 mg	ABRO 200 mg
	n (%)	n (%)	n (%)	n (%)		
With any adverse event	22 (16.8)	47 (19.7)	67 (29.6)	41 (16.9)	1.17 (0.8, 1.7)	1.66 (1.18, 2.35)
Gastrointestinal disorders	5 (3.8)	8 (3.4)	28 (12.4)	9 (3.7)	0.9 (0.35, 2.3)	3.16 (1.53, 6.56)
Nausea	2 (1.5)	5 (2.1)	23 (10.2)	5 (2.1)	1.02 (0.3, 3.47)	4.68 (1.81, 12.1)
General disorders and administration site conditions	1 (0.8)	8 (3.4)	8 (3.5)	6 (2.5)	1.36 (0.48, 3.85)	1.36 (0.48, 3.85)
Infections and infestations	12 (9.2)	24 (10.1)	20 (8.8)	19 (7.9)	1.28 (0.72, 2.28)	1.07 (0.59, 1.95)
Conjunctivitis	1 (0.8)	1 (0.4)	1 (0.4)	6 (2.5)	0.17 (0.02, 1.4)	0.17 (0.02, 1.4)
Folliculitis	3 (2.3)	0	1 (0.4)	1 (0.4)	NE	1.02 (0.06, 16.16)
Herpes simplex	0	2 (0.8)	5 (2.2)	0	NE	NE
Herpes zoster	NR	NR	NR	NR	—	—
Nasopharyngitis	3 (2.3)	9 (3.8)	4 (1.8)	5 (2.1)	1.83 (0.62, 5.38)	0.81 (0.22, 2.99)
Investigations	4 (3.1)	5 (2.1)	10 (4.4)	4 (1.7)	1.27 (0.35, 4.68)	2.54 (0.81, 7.99)
Natural killer cell count decreased	NR	NR	NR	NR	—	—
Nervous system disorders	0	4 (1.7)	14 (6.2)	4 (1.7)	1.02 (0.26, 4.02)	3.56 (1.19, 10.66)
Dizziness	0	1 (0.4)	5 (2.2)	0	NE	NE
Headache	0	2 (0.8)	8 (3.5)	4 (1.7)	0.51 (0.09, 2.75)	2.03 (0.62, 6.66)
Psychiatric disorders	0	1 (0.4)	5 (2.2)	1 (0.4)	1.02 (0.06, 16.16)	5.08 (0.6, 43.19)
Respiratory, thoracic and mediastinal disorders	4 (3.1)	1 (0.4)	2 (0.9)	1 (0.4)	1.02 (0.06, 16.16)	2.03 (0.19, 22.28)
Skin and subcutaneous tissue disorders	3 (2.3)	9 (3.8)	9 (4.0)	7 (2.9)	1.31 (0.49, 3.45)	1.31 (0.49, 3.45)
Acne	0	4 (1.7)	8 (3.5)	2 (0.8)	2.03 (0.38, 11)	4.07 (0.87, 18.96)

Source: Table 2.6.15, p57 of the submission

ABRO = abrocitinib; DUPI = dupilumab; NE = Not evaluable; NR = Not reported; PBO = Placebo; Q2W = Once every 2 weeks; QD = Once Daily; TEAE = treatment-related adverse event.

Included data up to 28 days after last dose of study. Incidence of ≥2% referred to ≥2% in any study arm. Subjects were counted only once per treatment per event. MedDRA v22. (JADE COMPARE) coding dictionary applied.

Table 8: Summary of treatment-related TEAEs (≥2%) from JADE DARE

	JADE DARE		Relative Risk ABRO vs DUPI (95% CI)
	ABRO 200 mg QD (N=362)	DUPI 300 mg Q2W (N=365)	
	n (%)	n (%)	
With any adverse event	125 (34.5)	57 (15.6)	2.21 (1.68, 2.92)
Gastrointestinal disorders	61 (16.9)	6 (1.6)	10.25 (4.49, 23.41)
Nausea	61 (16.9)	6 (1.6)	10.25 (4.49, 23.41)
General disorders and administration site conditions	NR	NR	-
Infections and infestations	31 (8.6)	38 (10.4)	0.82 (0.52, 1.29)
Conjunctivitis	5 (1.4)	28 (7.7)	0.18 (0.07, 0.46)
Folliculitis	8 (2.2)	1 (0.3)	8.07 (1.01, 64.17)
Herpes simplex	8 (2.2)	2 (0.5)	4.03 (0.86, 18.86)
Herpes zoster	9 (2.5)	2 (0.5)	4.54 (0.99, 20.85)
Nasopharyngitis	NR	NR	—
Investigations	9 (2.5)	0	NE
Natural killer cell count decreased	9 (2.5)	0	NE
Nervous system disorders	26 (7.2)	9 (2.5)	2.91 (1.38, 6.13)
Dizziness	NR	NR	-
Headache	26 (7.2)	9 (2.5)	2.91 (1.38, 6.13)
Psychiatric disorders	NR	NR	—
Respiratory, thoracic and mediastinal disorders	NR	NR	—
Skin and subcutaneous tissue disorders	39 (10.8)	9 (2.5)	4.37 (2.15, 8.89)
Acne	39 (10.8)	9 (2.5)	4.37 (2.15, 8.89)

Source: Table 2.6.15, p57 of the submission

ABRO = abrocitinib; DUPI = dupilumab; NE = Not evaluable; NR = Not reported; PBO = Placebo; Q2W = Once every 2 weeks; QD = Once Daily; TEAE = treatment-related adverse event.

Included data up to 28 days after last dose of study. Incidence of ≥2% referred to ≥2% in any study arm. Subjects were counted only once per treatment per event. MedDRA v24.0 (JADE DARE) coding dictionary applied.

- 6.37 The evaluation, the PSCR and the ESC agreed that ABRO and DUPI have different safety profiles. The PSCR stated that the higher rates of adverse events in the ABRO 200 mg arm compared to the ABRO 100 mg arm and the DUPI arm in JADE COMPARE and JADE DARE were influenced by the large number of nausea related events, and that these can be minimised by taking ABRO with food. The ESC disagreed with the assertion in the PSCR, noting that other adverse events were also higher for patients in the ABRO 200 mg arm.
- 6.38 The PSCR also stated that the Product Information recommends that patients with a higher risk of VTE, MACE and malignancy take the 100 mg dose of ABRO, and that the 200 mg dose may be appropriate for patients with high disease burden who are not at risk for these events. The ESC considered this inherently acknowledges that ABRO 200 mg has less favourable safety compared to ABRO 100 mg.
- 6.39 Treatment duration was short in the key head-to-head trials, which does not reflect the proposed long-term use of AD treatments. In addition, the study populations were too small to capture rare adverse events (AEs) associated with use of JAK inhibitors. Post market surveillance data for ABRO was not provided in the submission.

- 6.40 ABRO is included in the black triangle scheme. The ABRO product information (PI) includes warnings based on data from a post-market safety study of tofacitinib, another JAK inhibitor. AEs of interest associated with use of JAK inhibitors in the ABRO PI include but are not limited to serious infections (herpes simplex, herpes zoster, and pneumonia), VTEs including pulmonary embolism, and malignancy. The PI states that that ABRO should only be used if no suitable treatment alternatives are available in patients with risk factors for these events. Laboratory monitoring (complete blood count including platelet count, absolute lymphocyte count, absolute neutrophil count and haemoglobin; lipid parameters to monitor for hyperlipidaemia) is required 4 weeks prior to and after treatment initiation with ongoing monitoring based on assessment of patient risk factors. Recommendations are for use of the lowest effective dose of ABRO for maintenance treatment after establishing disease control.
- 6.41 Regulatory approval of ABRO by the TGA in April 2024 followed consideration by the Advisory Committee on Medicines (ACM) dating back to December 2021 and included a Section 60 review and an application to the Administrative Appeals Tribunal (AAT) (Act 1975) for a review of the Delegate’s decision. The main concerns were around the negative benefit-risk profile of ABRO including uncertainty over safety associated with use of JAK inhibitors and lack of adequate supporting data. ABRO was approved for the current indication after these concerns were adequately addressed by the applicant through the provision of additional data, and amendments to the Product Information for ABRO.
- 6.42 With respect to longer term safety information, the PSCR included a comparison of extension data from JADE EXTEND with population-based AD cohort studies. The PSCR suggested that this data indicates that the incidence rate for MACE, VTE and malignancies (excluding NMSC) reflects the rates of these events in patients with AD. The ESC considered that the value of the presented comparisons between long term safety data cohort and the population cohort data was limited and that it was difficult to draw conclusions due to a lack of matching.

Benefits/harms

- 6.43 A benefits and harms table is not presented as the submission made a claim of non-inferior efficacy and non-inferior safety for ABRO 200 mg versus DUPI 300 mg and an inferior efficacy and non-inferior safety claim for ABRO 100 mg versus DUPI 300 mg.

Clinical claim

- 6.44 The efficacy clinical claims were based on *post hoc* analyses of subgroups with severe AD (defined as IGA=4), with or without prior systemic treatment for AD, for a composite endpoint $EASI_{50}+DLQI \geq 4$. The clinical claim in the submission was that:
- ABRO 200 mg is non-inferior in terms of efficacy and non-inferior in terms of safety compared to DUPI 300 mg.
 - ABRO 100 mg is “not non-inferior” in terms of efficacy and non-inferior in terms of safety compared to DUPI 300 mg. The clinical claim for ABRO 100 mg would best

be expressed as ABRO 100 mg is inferior in terms of efficacy compared to DUPI 300 mg.

- 6.45 Overall, the ESC considered the claim that ABRO 200 mg is non-inferior in efficacy to DUPI 300 mg was supported by the evidence presented. The ESC further considered that the claim that ABRO 100 mg is “not non-inferior” (inferior) in efficacy to DUPI 300 mg was supported by the evidence presented, noting however, that the magnitude of difference between treatments is uncertain.
- 6.46 The ESC noted that the incidence of treatment-related TEAEs was higher in the ABRO 200 mg arm (29.6%) than in the ABRO 100 mg arm (19.7%) and the DUPI 300 mg arm (16.9%) in JADE COMPARE; the same trend was observed for ABRO 200 mg versus DUPI 300 mg in JADE DARE (34.5% vs. 15.6%). The ESC considered that the claim of non-inferior safety of ABRO 100 mg compared with DUPI 300 mg may be supported by the evidence presented in the submission, but the claim of non-inferior safety of ABRO 200 mg compared with DUPI 300 mg was not adequately supported by the evidence presented in the submission.
- 6.47 The ESC noted that safety comparisons were limited by patient numbers that were too small to capture rare AEs and the short treatment in the trials. The ESC noted that the adverse event profiles differed, with DUPI having higher rates of conjunctivitis and that numerically there were more adverse events with ABRO 200 mg: in particular, higher rates of herpes simplex, herpes zoster, folliculitis, nausea, acne and laboratory abnormalities.
- 6.48 The PBAC considered that the claim of inferior comparative effectiveness for abrocitinib 100 mg and non-inferior comparative effectiveness for abrocitinib 200 mg was reasonable. The PBAC noted the submission did not specifically make a claim in relation to abrocitinib 50 mg.
- 6.49 The PBAC considered that the claim of non-inferior comparative safety was reasonable for abrocitinib 100 mg, but that the claim was not adequately supported by the data for abrocitinib 200 mg. The PBAC note the submission did not specifically make a claim in relation to abrocitinib 50 mg.

Economic analysis

- 6.50 Based on the clinical claim of non-inferiority of ABRO 200 mg QD vs DUPI 300 mg Q2W, the submission presented a cost-minimisation approach (CMA). In addition, the submission made a claim of inferior efficacy and non-inferior safety of ABRO 100 mg vs DUPI 300 mg Q2W and presented a stepped cost-utility analysis (CUA) in which the model reported on a cost saving per responder missed, and per quality adjusted life year (QALY) forgone. The PSCR commented that the approach “was developed with reference to previous assessments [of cost-effectiveness] for the same patient population presented to PBAC for DUPI and for UPA, which... provided a consistent framework for PBAC to evaluate the cost-effectiveness of ABRO”.

- 6.51 The ESC considered the approach taken was consistent with the clinical claims for ABRO. However, the ESC considered that an alternative approach would be to present a combined model for the 100 mg, 200 mg and 50 mg doses, and transitions between them. The PSCR and pre-PBAC response argued that attempting to model all possible clinical scenarios would increase the complexity of the model and introduce considerable uncertainty where scenarios were misaligned with the clinical trial program for the medicines and therefore no reliable evidence would be available to inform the inputs. The PSCR and pre-PBAC response also noted that UPA also has a low dose (15 mg) and a high dose (30 mg) and the PI recommends a similar approach to titration to the lowest effective dose.
- 6.52 The ESC noted that the proposed DPMQ for the 100 mg dose of ABRO based on the CUA is 1/2 of the DPMQ for the 200 mg dose. In addition, the requested price for the 50 mg dose was equal to the requested price for the 100 mg dose. The ESC noted that the submission did not provide justification for the price of the 50 mg dose and considered that efficacy for the 50 mg dose is unlikely to be equivalent to the 100 mg dose given the clear dose response between the 100 mg and 200 mg doses. The ESC also noted that there is potential for patients to use multiple tablets (temporarily) where a dose increase is needed, which would result in a substantially increased cost compared with the cost for 200 mg tablets. The ESC advised that the PBAC may wish to consider whether pricing for the 50 mg, 100 mg and 200 mg doses of ABRO based on a constant cost per mg may be more appropriate. The pre-PBAC Response stated that “the 50 mg dose is recommended for patients taking strong inhibitors of CYP2C19 and those patients with moderate to severe renal impairment. In patients with these pharmacokinetic issues, the effect of the 50 mg dose on a patient’s AD is likely to be higher than a 50 mg dose in a patient without these pharmacokinetic interactions. The assertion that the 50 mg dose should be priced at half the 100 mg dose is inappropriate and is not reflective of the effects (outcome) of this dose on the population it is intended for”. No clinical data were provided for use of the 50 mg dose and the proposed restrictions did not limit treatment with the 50 mg dose to patients taking strong inhibitors of CYP2C19 or patients with moderate to severe renal impairment. The 50 mg ABRO dose accounted for 9-13% of total scripts in the financial estimates.

Cost-minimisation approach

- 6.53 The CMA was supported by the 16-week responder results (based on a post hoc analysis of PBS responder definition of EASI 50 + DLQI \geq 4) of the ABRO 200 mg arm vs the DUPI 300 mg Q2W arms of the JADE COMPARE study. For patients who remain on the 200 mg dose of ABRO, the ESC noted the CMA was consistent with that accepted by the PBAC for UPA 15 mg or 30 mg versus DUPI 300 mg, and considered the approach was generally reasonable, noting there is uncertainty around long-term comparative safety and effectiveness.
- 6.54 The CMA only included the cost of DUPI and ABRO 200 mg. No costs associated with adverse events or monitoring were included. Although the submission claimed that

the safety of ABRO 200 mg was non-inferior to DUPI, the ESC considered this may not be supported, and remains uncertain particularly for longer term safety. Further, the ESC noted that non-inferior safety does not necessarily mean equal management cost for AEs. As adverse events reported in JADE COMPARE were typically lower grade, the incremental cost of managing the different adverse event profiles of ABRO vs DUPI would be minimal over the duration of the JADE COMPARE study (16 weeks). The PSCR stated that omitting the costs of specific adverse events was consistent with the claim of non-inferiority and that this was consistent with the approach presented to the PBAC for UPA.

- 6.55 In addition, it is recommended in the ABRO Product Information (PI) that testing for hepatitis B, hepatitis C and tuberculosis occurs prior to treatment, and blood examinations occur prior to and during treatment. No recommendations for testing or monitoring appear in the DUPI PI. Although the cost of testing was not included in the CMA, the cost of testing and monitoring included in the CUA amounted to less than \$300 over two years.
- 6.56 The CMA estimated the equi-effective doses over 2 years assuming 100% relative dose intensity (RDI). The submission stated that it was not reasonable to compare monthly doses because DUPI has a single loading dose (600 mg) at the beginning of treatment. The RDI in JADE COMPARE was 94.9% for ABRO 200 mg and 93.4% for DUPI. Adjusting for RDI would have a minor impact on the CMA results. The CMA did not consider the impact of wastage associated with dose changes (for example, a reduction in the dose of abrocitinib 200 mg QD to 100 mg QD).
- 6.57 The ESC noted that the possibility of dose titration for both ABRO and DUPI was not accounted for in the CMA, and that there is some indication that in practice, dose intervals may be lengthened for patients responding well to Q2W DUPI. The ESC considered that accounting for dose titration for both ABRO and DUPI in the CMA may better reflect clinical practice, but was potentially complex and would depend on the price accepted for the 100 mg dose of ABRO, as the price proposed in the submission was not 1/2% of the 200 mg dose price.
- 6.58 The submission used the published price of DUPI in the CMA. The CMA presented in the submission was consistent with the approach accepted by the PBAC for the comparison of UPA 15 mg or 30 mg vs DUPI 300 mg Q2W (para 6.51-6.53 and 9.1, UPA PSD, July 2021 PBAC meeting and addendum).

Table 9: Results of the cost-minimisation approach using the published price of dupilumab

Component	Abrocitinib	Dupilumab
Cost per pack (AEMP)	\$1,640.82	\$1,609.86
Treatment duration per pack	4 weeks	4 weeks
Loading dose duration per pack	-	2 weeks
Dose duration (minus loading dose)	104 weeks	102 weeks
Cost of loading dose	-	\$1,609.86
Cost of treatment for 2 years (without loading dose)	\$42,661.29	\$41,051.43
Total cost of treatment for 2 years	\$42,661.29	\$42,661.29

Source: Section 3.4, pp88-9 of the submission.

AEMP = Approved ex-manufacturer price

6.59 Should the PBAC accept the clinical claim of overall non-inferior effectiveness and safety, the cost-minimisation approach must establish that the cost per patient for treatment with ABRO 200 mg would be no more than the cost per patient of DUPI 300 mg Q2W. Where these cost per patient calculations are uncertain, the guiding principle is that the Australian Government should not bear the financial risk of this uncertainty because the Australian population already has access to therapy that is at least as effective and safe. The commentary considered the key uncertainties of the CMA relate to long term comparative effectiveness and safety of ABRO vs DUPI.

Cost-utility analysis

6.60 The submission presented a modelled cost-utility analysis comparing ABRO 100 mg vs DUPI 300 mg Q2W. Of the patients who would receive abrocitinib in the Australian setting, the submission expected that more than two-thirds would receive the 100 mg dose. The structure was split between a 16-week decision-tree and a 5-year Markov state transition model. The time horizon of the decision-tree aligned with the proposed timing of the PBS continuation criteria. The ESC considered that while assessment of response at 16 weeks may favour ABRO given its earlier onset of action, assessment at this timepoint was reasonable as DUPI requires assessment of treatment response at 16 weeks. The ESC further considered that a 5-year duration for the Markov model was reasonable as it was consistent with other PBAC considerations for this indication.

6.61 The Markov model had two health states: responder and non-responder. The ESC agreed that the omission of mortality was a minor issue and unlikely to have significant impact. Responders received active treatment with ABRO 100 mg or DUPI 300 mg. Patients could either lose response (through treatment waning) or discontinue treatment (for reasons other than non-response), and transition to become non-responders.

6.62 The commentary considered the applicability of the model was unclear. The ABRO PI recommends the use of the lowest dose of ABRO required to achieve a response whereas the model compares a static 100 mg ABRO dose with DUPI. In clinical practice, many patients receiving ABRO 100 mg, who become non-responders, are likely to be prescribed and respond to ABRO 200 mg, rather than discontinuing ABRO. Additionally, the ESC considered that in clinical practice the dose of ABRO would be

titrated to the minimum dose that is effective, so some patients receiving the 100 mg dose would have been titrated down from the 200 mg dose. The ESC considered the model structure was too simple to adequately compare ABRO 100 mg vs DUPI 300 mg. A more accurate approach of estimating the cost-effectiveness of ABRO would be to compare the use of ABRO in clinical practice with the use of DUPI in clinical practice. Such an approach would capture the number of responders associated with dose titration (up and down) for ABRO, and may also capture whether the timing between DUPI doses is also varied. The ESC noted that there was no clear data to inform rates of up or down titration and response, and considered the direction of bias for this issue was unclear.

6.63 The ESC noted the structure of the Markov model presented was unidirectional whereas in clinical practice patients who discontinue treatment with DUPI or ABRO (for reasons other than lack of response) could reinitiate treatment and achieve a response, and the model did not allow for this. The ESC considered the direction of bias to be unclear.

6.64 Key inputs and methods used in the economic model are presented in Table 10.

Table 10: Summary of model structure, key inputs and rationale

Component	Summary
Treatments	ABRO 100 mg vs DUPI 300 mg Q2W
Time horizon	5.3 years in the model base case versus 16 weeks in JADE COMPARE
Outcomes	Responders (by PBS criteria – EASI 50 + DLQI \geq 4) QALYs
Methods used to generate results	16-week decision tree 5-year Markov model
Health states	Responder and non-responder
Cycle length	Following the decision tree component, 6 months
Transition probabilities	Responders at 16 weeks derived from JADE COMPARE Loss of treatment response informed by JADE EXTEND (at 48 weeks) and a previous consideration of DUPI (Table 19, DUPI, PSD, March 2020 PBAC meeting) (at 42 weeks) Discontinuation informed by JADE EXTEND
Extrapolation method	At 16 weeks, patients not achieving the PBS continuation criteria become non-responders. Each cycle of the cohort model, a proportion of remaining responders become non-responders either through discontinuation or through loss of treatment effect (which leads to discontinuation). More than 90% of the incremental QALY losses, and more than 70% of the incremental cost savings occurred after the 16-week decision tree component.
Health related quality of life (utilities)	<ul style="list-style-type: none"> • Baseline (up to week 8): 0.6 • Responders between week 9 and week 16: 0.847 • Responders between week 17 and week 42: 0.91 • Responders from week 43: 0.79 • Non-responders (any time): 0.6

Source: Table 3.5.1, pp91-2, Table 3.7.1, p105 of the submission.

ABRO = abrocitinib; DLQI = Dermatology Life Quality Index; DLQI \geq 4 = Proportion of patients with improvement in baseline DLQI of \geq 4 points from baseline; DUPI = dupilumab; EASI = Eczema Assessment Severity Index; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PSD = Public Summary Document; Q2W = Once every 2 weeks; QALY = Quality-adjusted life-year

6.65 Initial treatment effectiveness was sourced from a post hoc analysis of 16-week results from JADE COMPARE. The analysis was performed to match the PBS definition of

responder (EASI 50 + DLQI \geq 4), and to narrow the population to the severe subgroup (IGA=4 at baseline) without prior use of systemic immunosuppressants. The analysis indicated that, at 16 weeks, 65.7% and 71.4% of patients receiving ABRO 100 mg and DUPI 300 mg, respectively, had achieved response using the PBS definition of response. Although these results were generated using a post hoc analysis, they were not inconsistent with the small advantage of DUPI 300 mg over ABRO 100 mg observed for other study outcomes.⁵

- 6.66 As not all patients responded immediately to treatment, the decision-tree component made a simplifying assumption and assumed all responders by 16 weeks achieved response at 8 weeks. This approach may underestimate response in both arms, but as patients receiving DUPI appeared to take longer to respond, this approach may have slightly disadvantaged the ABRO arm.
- 6.67 At 16 weeks, all non-responders were modelled to discontinue. Between 16 weeks and 5.3 years, patients in the response health state transitioned to non-response due to discontinuation or due to a loss of treatment effect. The rates of discontinuation (6.3% per year) were derived from the JADE EXTEND study at 48 weeks and applied to 5.3 years. The derivation of the rates was unclear, and the post hoc analysis could not be identified in the submission supporting documents. No evidence to support a static rate of discontinuation over 5 years was provided. The same discontinuation rate was applied to both the ABRO 100 mg and DUPI arms of the model. DUPI was not included in the JADE EXTEND study and no evidence to support a similar discontinuation rate was provided in the submission. The model was not sensitive to changes in the discontinuation rate, but was sensitive if the discontinuation rates differed across arms. The PSCR stated that a recent publication of real-world evidence (RWE) for DUPI in Danish patients supports the assumption that both ABRO and DUPI (which reported 86% drug survival at 2 years) have similar discontinuation rates (Vitrup 2023), and that this value aligns with the persistence modelled for ABRO and DUPI in the CUA of “88% at 1.8 years and 85% at 2.3 years”. The ESC considered that dropout rates based on RWE are likely to be higher than in trials.
- 6.68 Loss of treatment effect (treatment waning) was informed by the JADE EXTEND study at 48 weeks and from the DUPI PSD (Table 19, DUPI, PSD, March 2020 PBAC meeting). The submission assumed that 5% of responders would become non-responders each cycle and that this rate was the same across both arms. This approach results in 100% loss of treatment effect at 10 years. The ESC considered it was not reasonable to apply loss of treatment effect measured at 48 weeks in the trial across 5 years.
- 6.69 The loss of treatment effect appeared to be greater in the ABRO 100 mg arm of JADE EXTEND (9.5% at 48 weeks) than was reported for DUPI (4.3% at 42 weeks, Table 16,

⁵ Note that the results presented in Paragraphs 6.65, 6.67 and 6.69 are derived from post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plans for JADE COMPARE or JADE DARE. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

DUPI PSD, March 2020 PBAC meeting). In addition, the ESC noted that the loss of treatment effect was substantially higher for patients treated with the 100 mg dose who had severe AD (IGA4) and no prior immunomodulatory therapy (71.4% response at week 48), however data from this small subgroup was potentially unreliable. The PSCR stated that “the assumption of linear waning over 10 years results in a proportion sustaining response of 95% after 42 weeks of treatment with ABRO, which is within the range of sustained response rates of 90.5% to 100% observed in JADE EXTEND. Similarly, those who were responders to DUPI at Week 16 sustained response at similar rates: Week 42 (95.7%) and at Week 68 91.2% (PSD March 2020; Table 19), confirming that it was reasonable to assume similar rates of treatment waning”. The model was sensitive to differential estimates of treatment waning. The ESC considered the submission’s assumptions regarding equal treatment waning for both treatment arms to be uncertain and not well-supported by the clinical data. The ESC noted that an assumption of non-linear treatment waning favoured ABRO and had a significant impact on the ICER. The ESC noted that when different rates of treatment waning were applied to ABRO and DUPI arms based on the trial response rates the ICER worsened, decreasing to a saving of \$45,000 to < \$55,000 per QALY forgone.

- 6.70 Health state utilities were sourced from the DUPI March 2020 PSD (Table 13, DUPI, PSD, March 2020 PBAC meeting). The submission claimed that the HRQoL outcomes from the JADE trials were less applicable to the proposed population as the trials excluded patients with substantial mental health issues (such as depression). The utility estimates from the JADE trials for non-responders were higher than those from the previous consideration of DUPI. As there were a greater number of non-responders in the ABRO 100 mg arm of the model, applying a lower utility value for the non-responder health state would disfavour the ABRO arm. The commentary considered the approach taken was reasonable.
- 6.71 The ESC noted that patients receiving DUPI who have a long-term response may seek to increase the duration between doses, with emerging evidence suggesting some patients may have ongoing durable responses with less frequent DUPI dosing. The ESC noted that this was not accounted for in the modelled drug costs. The ESC considered down titration of dose may also occur for patients treated with ABRO, however the comparative reduction in costs for ABRO may not be as great due to the proposed flat pricing between the 50 mg and 100 mg dose and the relatively small price difference between the 100 mg and 200 mg doses. The pre-PBAC response noted that no evidence was available to support this assertion and increasing the duration of DUPI doses is not within the DUPI PI.
- 6.72 The model included costs for monitoring (prior to and during the use of ABRO), adverse event costs, healthcare costs for the management of responders and non-responders, and a small cost applied immediately following treatment failure to account for the use of other systemic medications. Other costs included in the model were small compared with the cost of ABRO and DUPI. The largest non-drug cost was the annual cost of health care for responders and non-responders. These costs were

sourced from the DUPI PSD March 2020 (Table 13, DUPI, PSD, March 2020 PBAC meeting). As recommended by PBAC during its consideration of UPA (Table 12, UPA PSD, July 2021 PBAC meeting), the costs of phototherapy were removed. The commentary considered the costs included in the model were reasonable. The model was not sensitive to changes in costs (other than the price of ABRO and DUPI).

6.73 The sponsor applied a hypothetical price of \$ [REDACTED] (AEMP) for DUPI. The price applied in the model for ABRO was \$ [REDACTED] (AEMP).

Table 11: Key drivers of the model

Description	Method/Value	Impact Base case: \$ [REDACTED] saving per QALY forgone
Discontinuation	Discontinuation rates were derived from the 48 week follow up in JADE EXTEND, and were applied over 5 years, and assumed to be the same for DUPI.	High, does not inherently favour either arm. There is no evidence that the discontinuation rate is constant over time, nor that the discontinuation rate for ABRO up to 48 weeks can be used for DUPI. The model is sensitive to small differences in discontinuation across the arms.
Loss of treatment effect	The preservation of treatment effect was informed by results from JADE EXTEND for ABRO (90.5% at 48 weeks) and Table 19, dupilumab PSD, March 2020 PBAC meeting) (95.7% at 42 weeks). The model assumed the same loss of treatment effect of 5% per 6-month cycle.	High, likely favours the ABRO arm. Using treatment arm specific estimates results in a reduction of the cost-savings per QALY forgone of 42.6%.

Source: Generated from the abrocitinib economic evaluation model

ABRO = abrocitinib; DUPI = dupilumab; PBAC = Pharmaceutical Benefits Advisory Committee; PSD = Public Summary Document; QALY = Quality-adjusted life-year

The redacted values correspond to the following ranges:

¹ \$75,000 to < \$95,000

6.74 The submission base case estimated a \$75,000 to < \$95,000 saving for each QALY forgone. The ESC noted the lack of PBAC precedents for incremental cost-effectiveness ratios (ICERs) where there was a cost saving per QALY forgone, which makes the interpretation of what is an acceptable ICER difficult.

Table 12: Stepped derivation of the base-case economic evaluation from the study data

	Outcome / population	Incremental costs (\$)	Incremental outcomes (%)	Cost saving per health forgone
Trial based: 16 weeks				
Step 1: EASI 75, mITT	Responder	-████	-5.20%	\$████ saved/ responder missed
Step 2: EASI 75, severe subgroup	Responder	-████	-4.20%	\$████ saved/ responder missed
Step 3: EASI 50 + DLQI≥4, severe subgroup	PBS continuation criteria responder	-████	-5.70%	\$████ saved/ responder missed
Extrapolated: 16 weeks + 5 years				
Step 4: EASI 50 + DLQI≥4, severe subgroup	PBS continuation criteria responder	-████	-5.70%	\$████ saved/ responder missed
Step 5: As above, utility weights attached.	QALY	████ ¹	-0.0431	\$████ ² saved/ QALY lost
Base case				
Step 6: As above, discounted 5% p.a. [Base case economic evaluation]	QALY	████ ¹	-0.0399	\$████ ² saved/ QALY lost

Source: Table 3.12.2, p115 of the submission.

DLQI = Dermatology Life Quality Index; DLQI≥4 = Proportion of patients with improvement in baseline DLQI of ≥4 points from baseline; EASI = Eczema Assessment Severity Index; mITT = modified intent to treat; PBS = Pharmaceutical Benefits Scheme; QALY = Quality-adjusted life-year

The redacted values correspond to the following ranges:

¹ Dominant

² \$75,000 to < \$95,000

- 6.75 The ESC considered that there was inherent uncertainty regarding the ICER because the magnitude of difference between 100 mg ABRO and DUPI was uncertain due to the limitations of the evidence related to the post hoc nature of the analyses in small subgroups.
- 6.76 The model was primarily sensitive to assumptions regarding treatment waning (loss of treatment effect over time that resulted in the transition from responder to non-responder) and to the estimate of discontinuation. These two estimates (treatment waning and discontinuation rates) are highly uncertain, particularly the assumption that they are the same in both arms over the duration of the model. No long-term data were provided to support the model predictions in terms of either long-term discontinuations or long-term treatment effect. The assumption that discontinuations and loss of treatment effect was the same across treatment arms forced the convergence of the responder curves (as applying the same proportional loss of treatment effect or discontinuation in the DUPI arm results in a larger absolute number of transitions to nonresponse, as the starting proportion of responders is higher).

Table 13: Results of sensitivity analyses performed during the evaluation

	Analyses	Incremental cost	Incremental QALY	ICER
	Base case	-\$ [redacted]	-0.0399	[redacted] ¹
	Time horizon (base case: 5 years)			
	2 years	-\$ [redacted]	-0.0243	[redacted] ²
	10 years	-\$ [redacted]	-0.0471	[redacted] ¹
	Discontinuation (base case: 6.3% per annum for both ABRO and DUPI)			
1	6.3% for ABRO, 5% for DUPI	-\$ [redacted]	-0.0503	[redacted] ¹
	Treatment waning (base case: 10 years, or 5% per cycle for both ABRO and DUPI)			
2	6.46 years for ABRO, 11.63 years for DUPI ^a	-\$ [redacted]	-0.1206	[redacted] ³
	Costs (base case DPMQ for ABRO and DUPI and MBS item 23 based on July 2024 prices)			
	DPMQ updated (August prices)	-\$ [redacted]	-0.0399	[redacted] ¹
	MBS 23 updated (August prices)	-\$ [redacted]	-0.0399	[redacted] ¹
	Safety (safety rates for ABRO 200 mg used)			
	Use safety rates for ABRO 100 mg	-\$ [redacted]	-0.0399	[redacted] ¹
	Multivariate analysis			
1+2	Discontinuation and waning	-\$ [redacted]	-0.1319	[redacted] ³

Source: generated during the evaluation from the ABRO economic model spreadsheet.

ABRO = abrocitinib; DPMQ = Dispensed Price for Maximum Quantity; DUPI = dupilumab; ICER = Incremental cost-effectiveness ratio; MBS = Medicare Benefits Schedule; QALY = Quality-adjusted life-year

^aTime until treatment response becomes zero is derived from 90.5% response at 48 weeks (ABRO) and 95.7% response at 42 weeks (DUPI).

The redacted values correspond to the following ranges:

¹ \$75,000 to < \$95,000

² \$95,000 to < \$115,000

6.77 ³ \$45,000 to < \$55,000 When treatment waning was altered in the model to reflect the loss of treatment effect reported in JADE COMPARE for ABRO 100 mg (90.5% at 48 weeks) and Table 19, DUPI, PSD, March 2020 PBAC meeting for DUPI 300 mg (95.7% at 42 weeks), the cost-saving per QALY lost was reduced by more than 40% (analysis 2 in Table 13 above). Although this estimate better reflected the short-term data available, the long-term treatment waning of either ABRO or DUPI remains uncertain.

6.78 The ESC noted that the sensitivity analyses presented in the submission Table 14 showed the ICER was also sensitive to the assumptions relating to dose intensity, time to response, or whether patients have had prior immunomodulatory therapy (though this was based on data from a small number of patients).

Table 14: Univariate sensitivity analyses presented in the submission

Parameter setting		ICER (\$ saved per QALY forgone)			
Base case: ██████ ¹ /QALY SWQ		Lower	Upper	Difference from base case (/QALY forgone)	
Base case variable	Test variable				
IMM experience: no prior	prior	█████ ² SWQ	-	-█████ ³	-
Time to response ABRO and DUPI 8 weeks	ABRO 12 weeks; DUPI 12 weeks	█████ ⁴ SWQ	█████ ⁵ SWQ	-█████ ⁶	█████ ²
Dose intensity ABRO 94.9%, DUPI 93.4%:	ABRO 100% DUPI 100%	█████ ⁴ SWQ	█████ ⁵ SWQ	-█████ ⁶	█████ ²

Source: Section 3.13.2, p120 of the submission.

ABRO = abrocitinib; DUPI = dupilumab; EASI75 = Proportion of patients with improvement of ≥ 75% from baseline in Eczema Area and Severity Index; HCRU = health care resource utilisation ICER = Incremental cost-effectiveness ratio; IMM = Immunomodulatory; PSD = Public Summary Document; QALY = Quality-adjusted life-year; SWQ = south-west quadrant

The redacted values correspond to the following ranges:

- ¹ \$75,000 to < \$95,000
- ² \$45,000 to < \$55,000
- ³ \$35,000 to < \$45,000
- ⁴ \$55,000 to < \$75,000
- ⁵ \$135,000 to < \$155,000
- ⁶ \$25,000 to < \$35,000

Drug cost/patient/year

Table 15: Drug cost per patient for ABRO 200 mg and DUPI 300 mg Q2W

	Proposed drug Trial dose and duration	Proposed drug Model ^a	Proposed drug Financial estimates	Comparator Trial dose and duration	Comparator Model ^a	Comparator Financial estimates
Mean dose	189.8 mg ^b	200 mg QD	200 mg	280.2 mg Q2W ^c	300 mg Q2W	300 mg Q2W
Mean duration	106.3 days	2 years	-	104.6 days	2 years	-
Cost/patient/ year		\$█	\$█		\$█	\$█ (1 st year) \$█ (subsequent years)

ABRO = abrocitinib; DUPI = dupilumab; Q2W = every two weeks; QD = once daily.

^aCost per patient per year is estimated using published prices.

^bABRO 93.7% relative dose intensity. Mean dose was not provided in the JADE COMPARE clinical study report, and the mean dose in the trial has been estimated using the submission's reported RDI.

^cDUPI 93.4% relative dose intensity – dose does not include loading dose. Mean dose was not provided in the JADE COMPARE clinical study report, and the mean dose in the trial has been estimated using the submission's reported RDI.

Table 16: Drug cost per patient for ABRO 100 mg and DUPI 300 mg Q2W

	Proposed drug Trial dose and duration	Proposed drug Model ^c	Proposed drug Financial estimates ^d	Comparator Trial dose and duration	Comparator Model ^c	Comparator Financial estimates
Mean dose	93.7 mg ^a	93.7 mg QD ^a	100 mg	280.2 mg Q2W ^b	280.2 mg Q2W ^b	300 mg Q2W
Mean duration	104.9 days	2.55 years	-	104.6 days	2.75 years	-
Cost/patient/ year	-	\$█	\$█	-	\$█	\$█ (1 st year) \$█ (subsequent years)

ABRO = abrocitinib; DUPI = dupilumab; Q2W = every two weeks; QD = once daily.

^aABRO 93.7% relative dose intensity. Mean dose was not provided in the JADE COMPARE clinical study report, and the mean dose in the trial has been estimated using the submission's reported RDI.

^bDUPI 93.4% relative dose intensity – dose does not include loading dose. Mean dose was not provided in the JADE COMPARE clinical study report, and the mean dose in the trial has been estimated using the submission's reported RDI.

^cCost per patient per year is based on a hypothetical price of DUPI of \$█ (AEMP)

^dThe proposed published price of abrocitinib 100 mg is the same as that for abrocitinib 200 mg.

Estimated PBS usage & financial implications

6.79 This submission was not considered by DUSC. The submission used a mixed approach to estimate the financial implications associated with the listing of ABRO on the PBS as a once-daily treatment for moderate to severe atopic dermatitis in adults. A market share approach was used to capture the substitution from the existing market (DUPI and UPA). In addition, an epidemiological approach was used to capture patients supplied ABRO through a proposed patient familiarisation program who would transition to PBS supply once ABRO was available on the PBS.

Table 17: Key inputs for financial estimates

Data	Value	Source	Comment
Size of the market			
Total services for all strengths of currently listed DUPI and UPA for atopic dermatitis (May 2023 – April 2024)	DUPI: 166,511 UPA: 27,018 Total: 193,526	Medicare Statistics (May 2023 to April 2024) for PBS items: 12292Y (DUPI 300 mg injection), 12828E, 12831H, 12835M (UPA 15mg tablet) 12836N, 12829F, 12827D (UPA 30 mg tablet).	While the source for estimating the size of the market was appropriate, the standard approach is to use the last full calendar year for analysis. This ensures that any seasonality in the market is accounted for correctly. Use of the most recent data (financial year 2023/24) resulted in an increase in script volume of approximately 8%.
Phase of treatment adjustments	21.6% initiating 70.5% continuing 7.9% dose modification	The proportions of initial and continuing UPA scripts have been applied to the DUPI scripts.	DUPI scripts are not distinguished by initial and continuing phases of treatment in their item codes. The submission has broken the DUPI scripts into distinct treatment phases to allow the current DUPI scripts to be equated to the proposed ABRO scripts. As the UPA market is immature, this may have resulted in an over-estimation of the proportion of DUPI scripts used in initiation.

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Data	Value	Source	Comment
Patient age adjustments	<p>DUPI 3.87% children 77.69% adults</p> <p>UPA 22.31% children 77.69% adults</p>	<p>The proportion of currently treated patients who would be eligible for treatment with ABRO. The adjustment was based on the relative size of each age group as a proportion of the total Australian population in 2024 (ABS 3222.0 Series B).</p>	<p>The submission sought a listing for ABRO for adult patients (18 years and older); however, the current market also provides treatment for children 12 years and older. The UPA adjustment was correctly applied; however, the DUPI adjustment was incorrect as the overall population is patients from 2 years, not the entire population. This was corrected during the evaluation. Overall, the approach was reasonable, if the atopic dermatitis population has the same age distribution as the general population.</p>
Annual growth for current listing	<p>2.5% - 2024-25 2.2% - 2025-30</p>	<p>DUSC Cost-effectiveness review of drugs for atopic dermatitis (November 2023 PBAC).</p>	<p>The figure appears appropriate; however, it is not clear why the growth rate from 2024 to 2025 is 2.5%. The ESC considered the growth rate to be uncertain.</p>
Proportion applicable to indication	100%	Applicant assumption	<p>This approach is appropriate given the other adjustments that have been made in prior steps.</p>
Uptake rate	<p>DUPI █ % - █ %</p> <p>Upadacitinib █ % - █ % - █ %</p>	DUPI PSD Nov 2020	<p>The source and validity of these figures could not be determined as they linked to hard coded numbers in the UCM. The numbers could not be found in the reference provided by the applicant.</p>
Grandfathered patients	█ 1 patients annually	Applicant's proposed Patient Familiarisation Program.	<p>Grandfathered patients are included in financial estimates to account for patients outside of the market under consideration. The source of these patients was unclear - if they are treatment experienced, their utilisation will be captured in the current market as the PFP has not yet commenced. In revised estimates provided with the PSCR, grandfathered patients were removed in years 2-6 of the estimates.</p>
Continuation rate for grandfathered patients	78%	DUSC Cost-effectiveness review of drugs for atopic dermatitis (November 2023 PBAC).	<p>This continuation rate is appropriate between initial and continuing patients. The submission notes that grandfathered patients will only receive continuing treatment, which means that only 78 grandfathered patients will receive treatment. Additionally, there is no indication of the likely continuation rate for subsequent years of treatment. It is unlikely that once on continuing treatment, patients will remain on treatment indefinitely. The revised PSCR estimates did not include continuing treatment in grandfathered patients.</p>

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Data	Value	Source	Comment
Treatment utilisation			
Scripts dispensed	Yr 1: 2 Yr 2: 3 Yr 3: 4 Yr 4: 4 Yr 5: 4 Yr 6: 5	ABRO : DUPI (initial) = 0.93 ABRO : DUPI (cont) = 0.97 ABRO : UPA = 1	The derivation of the annual number of scripts per patient for DUPI contains an error where two injections are given in consecutive weeks rather than every two weeks. This error was corrected during the evaluation. The PSCR stated that this represents the DUPI loading dose. Inclusion of the loading doses in the first week was reasonable, however in the last two weeks of the first year (weeks 51 and 52), the UCM shows doses of dupilumab being administered. As dupilumab is administered every two weeks, this is incorrect and inconsistent with the dosing regimen used in the balance of the first year.
Costs			
Proposed medicine	\$1,416,19	Requested DPMQ (published price)	The DPMQ was calculated using the previous fees and mark-ups and was updated during the evaluation.
Affected medicine	\$1,755.19 \$1,272.31 \$2,077.29	12292Y 12828E, 12831H, 12835M 12836N, 12829F, 12827E	The DPMQs presented use the previous fees and mark-ups and were updated during the evaluation.
Patient copayment	\$24.94 PBS \$5.58 RPBS	Weighted copayments for PBS items: 12292Y (DUPI 200 mg and 300 mg injection), 12828E, 12831H, 12835M (UPA 15mg tablet), 12836N, 12829F, 12827D (UPA 30 mg tablet).	The co-payment information included in the financial estimates is correctly described, but incorrect figures have been presented in the submission main body, without affecting the overall calculations.
PBS: RPBS split	99.37%: 0.63%		
MBS costs	\$0	No MBS items were included in the financial estimates.	This is inconsistent with the submission that indicates that a range of tests are required prior to treatment with ABRO, together with monitoring items during each cycle of treatment with the proposed medicines.

Source: Compiled during the evaluation from Section 4 of the submission and the UCM.

ABS = Australian Bureau of Statistics; DPMQ = Dispensed Price for Maximum Quantity; DUSC = Drug Utilisation Sub Committee; MBS = Medicare Benefits Schedule; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PFP = Product Familiarisation Program; PSD = Public Summary Document; RPBS = Repatriation Pharmaceutical Benefits Scheme

The redacted values correspond to the following ranges:

¹ <500

² 500 to < 5,000

³ 5,000 to < 10,000

⁴ 10,000 to < 20,000

⁵ 20,000 to < 30,000

Table 18: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated financial implications of ABRO						
Abrocitinib 50 mg scripts (PBS/RPBS)	1	2	2	2	2	2
Abrocitinib 100 mg scripts (PBS/RPBS)	2	2	3	4	4	4
Abrocitinib 200 mg scripts (PBS/RPBS)	1	2	2	2	2	3
Impact to PBS/RPBS less copayments (\$)	5	5	6	7	7	8
Estimated financial implications of DUPI and UPA						
Impact to PBS/RPBS less copayments (\$)	9	9	9	9	9	9
Net financial implications						
Net impact to PBS/RPBS (\$)	9	9	9	9	9	9
Revised ^a (\$)	5	9	9	9	9	9
PSCR revised ^b (\$)	9	9	9	9	9	9

Source: Table compiled during evaluation from Excel workbook "ABRO UCM"

PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme

^a Values were corrected during the evaluation based on the following changes: updated current market script volumes to cover FY 2023-24; addition of 78 grandfathered patients receiving continuing treatment; updated script equivalence between proposed and affected medicines; updated fees and mark-ups for proposed and affected medicines to reflect 1 Jul 2024 values.

^b The PSCR updated the published and effective DPMQs using updated fees and mark-ups and revised the number of repeats to align with the proposed restriction, however corrections to the number of grandfathered patients and scripts and corrections to the script equivalence were not applied.

The redacted values correspond to the following ranges:

¹ < 500

² 500 to < 5,000

³ 5,000 to < 10,000

⁴ 10,000 to < 20,000

⁵ \$0 to < \$10 million

⁶ \$10 million to < \$20 million

⁷ \$20 million to < \$30 million

⁸ \$30 million to < \$40 million

⁹ net cost saving

6.80 The financial impact to the PBS/RPBS of listing ABRO was estimated to be a saving of \$0 to < \$10 million in Year 6, and a total saving of \$20 million to < \$30 million in the first 6 years of listing.

6.81 The financial estimates in the submission and PSCR were underestimated because the utilisation and cost model was not correctly used to generate the scripts (and hence the costs) associated with treating the grandfathered patients. This has the greatest impact in the initial years of listing where the grandfathered patients' scripts represent a greater proportion of the total cost.

6.82 While the submission is presented on a cost-minimisation basis for the 200 mg dose and with a cost saving proposed for the 100 mg dose, the listing results in a cost in the first year due to the inclusion of grandfathered patients. As these patients are otherwise untreated (even if they have previously been treated), there are no cost offsets applied to their treatment. This results in an overall cost to the PBS/RPBS in the first year that is highly sensitive to the size of the grandfathered patient

population. The submission assumed no additional growth in the market associated with the introduction of an additional treatment option.

- 6.83 The submission proposed a grandfathered patient population drawn from a proposed patient familiarisation program (PFP). The PFP was assumed to provide < 500 new grandfathered patients over each of the first six years of listing. These patients would continue treatment after the initial 16 weeks of treatment at a rate of 78%. The submission stated that grandfathered patients would not receive PBS-subsidised initial treatment as they would commence their treatment through the PFP. The commentary considered it was unclear what the source of initiating grandfathered patients would be beyond the first year of listing. It is also unclear why < 500 grandfathered patients have been included when the submission states that only continuing patients would access treatment and there is a 22% discontinuation rate between initial and continuing patients. The PSCR stated that the discontinuation rate for patients transitioning from non-PBS to PBS treatment in year 1 is uncertain and acknowledged that the assumptions may overestimate the patient numbers.
- 6.84 The financial estimates assumed that 61-72% of ABRO scripts in each year would be for the 100 mg dose and that 9-13% of total ABRO scripts in each year would be for the 50 mg dose. It was unclear how the split of ABRO doses was determined.

Financial Management – Risk Sharing Arrangements

- 6.85 The sponsor has indicated that they are willing to join the existing Risk Share Arrangement (RSA) that contains DUPI and UPA for the treatment of severe atopic dermatitis. This RSA was the subject of a DUSC review (September 2023) and a cost-effectiveness review of drugs for atopic dermatitis (November 2023 PBAC) and Category 3 PBAC submissions in July 2022 and July 2023. A delist request for DUPI was also considered in July 2024.
- 6.86 The sponsor did not request any changes to the caps associated with the existing DUPI / UPA RSA. As this listing will provide an alternative to the currently listed agents and treat the same patient populations, it is not expected to increase the size of the market and hence an increase in the RSA caps is not warranted.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the General Schedule Authority Required listing of abrocitinib (ABRO) 200 mg, 100 mg and 50 mg tablets for the treatment of adult patients with chronic severe atopic dermatitis (AD). The PBAC recommended the listings (doses) on the basis of the following cost-effectiveness considerations:
- ABRO 200 mg was recommended on the basis of a cost-minimisation approach (CMA) compared to dupilumab (DUPI). The PBAC considered the evidence presented in the submission demonstrated that ABRO 200 mg has non-inferior efficacy compared to DUPI. The Committee considered the equi-effective doses

were ABRO 200 mg orally once daily and DUPI 600 mg subcutaneously as an initial dose then 300 mg every 2 weeks thereafter assuming equivalent drug costs over a 2-year period. The PBAC considered that the cost effectiveness of abrocitinib 200 mg would be acceptable if it were cost-minimised to the lowest cost alternative therapy of DUPI or UPA.

- ABRO 100 mg was recommended on the basis of a cost-utility analysis (CUA) compared to DUPI. The PBAC considered that ABRO 100 mg provides an inferior clinical benefit to that of DUPI but that it may have a place in therapy for patients not responding to other systemic treatments who can't be treated with the higher ABRO 200 mg dose for safety reasons, and for patients who are responding to ABRO 200 mg and who want to down titrate to the lowest effective maintenance dose (as recommended in the ABRO Product Information (PI)). The Committee considered that ABRO 100 mg orally once daily would be cost-effective at a price that resulted in the cost saving per quality adjusted life year foregone of \$75,000 to < \$95,000 or more compared to DUPI.
 - ABRO 50 mg was recommended based on the Committee's consideration that the 50 mg strength of ABRO would be cost-effective at the same price per mg as the 100 mg strength, noting that the 50 mg dose is recommended for patients with moderate to severe renal impairment, or for those taking strong inhibitors of cytochrome P450 (CYP) 2C19. The PBAC noted that no evidence for the 50 mg ABRO dose was presented in the submission.
- 7.2 The PBAC acknowledged the clinical need for additional treatments for severe AD, noting the consumer comments that there was an example of a patient who had not responded to DUPI obtaining significant benefit from ABRO. The Committee considered there was a modest clinical need for ABRO, noting that it had a different mode of administration to DUPI and that it may be particularly valued by patients who fail to respond to, or do not tolerate, other systemic therapies for AD.
- 7.3 The PBAC noted that under the proposed listing, sequential use of PBS listed therapies for severe atopic dermatitis would be permitted and that the most appropriate sequence for their use has not been determined. The PBAC noted that both DUPI and upadacitinib (UPA) are listed on the PBS and considered it reasonable that ABRO should be available as a first-line option along with DUPI and UPA.
- 7.4 The PBAC noted that the proposed restrictions, in terms of disease severity and treatment response were consistent with those for DUPI and UPA, and considered this was appropriate. The PBAC considered it was reasonable to include restrictions allowing treatment with ABRO for patients with severe AD of the hands/face only, consistent with the existing listings for DUPI and UPA.
- 7.5 The PBAC noted that the submission proposed a maximum quantity of 1 pack of 28 units of either ABRO 200 mg, 100 mg or 50 mg with 3 repeats for initial treatment, allowing for up to 16 weeks of treatment to assess whether the patient achieves the required response for continuation. The PBAC noted that assessment of response at

16 weeks was consistent with the economic analyses and considered the number of repeats to be appropriate.

- 7.6 The PBAC noted that the submission stated that ABRO 100 mg once daily is the preferred dose for most patients and that it is the recommended maintenance dose. The submission stated that the 200 mg once daily dose may be appropriate for patients with a high disease burden who are not at high risk of venous thromboembolism (VTE), a major cardiovascular event (MACE) or malignancy, with patients decreasing to 100 mg once daily upon disease control. The PBAC noted that ABRO 50 mg once daily is the dose recommended for patients taking strong inhibitors of cytochrome P450 (CYP) 2C19 and/or patients with moderate or severe renal impairment. The PBAC considered it reasonable that a range of strengths of ABRO should be available, noting that the ABRO Product Information states that the tablets should not be split or crushed.
- 7.7 The PBAC noted the submission nominated DUPI 600 mg subcutaneously as an initial dose followed by 300 mg every 2 weeks thereafter as the main comparator, as it is the treatment most likely to be replaced by ABRO, and UPA (15 mg and 30 mg, taken once orally daily) as a supplementary comparator. The PBAC recalled that UPA was recommended for severe AD on a cost-minimisation basis to DUPI, following its July 2021 meeting. The PBAC considered that the nominated comparators were appropriate.
- 7.8 The PBAC noted that the submission was primarily based on two head-to-head randomised controlled trials comparing ABRO 200 mg once daily to DUPI 300 mg every 2 weeks (JADE COMPARE and JADE DARE), and one head-to-head RCT comparing ABRO 100 mg once daily to DUPI 300 mg every 2 weeks (JADE COMPARE), in patients with moderate to severe AD, and that supplementary evidence from two non-comparative ABRO studies, JADE REGIMEN and JADE EXTEND was also provided.
- 7.9 The PBAC noted the submission relied on the results of post hoc subgroup analyses of patients with severe AD (defined as IGA=4 at baseline) from JADE COMPARE (for ABRO 100 mg) and from the pooled results from JADE DARE and JADE COMPARE (for ABRO 200 mg) to inform the clinical claim, economic analyses and financial estimates. While the PBAC noted that the number of patients in these subgroups was small, data provided in the PSCR showed the groups were well balanced, and likely to be representative of the results for the severe AD subgroup for DUPI (defined by an IGA of 4 and EASI>20). As such, the Committee considered that the risk of bias associated with the use of the subgroups was reduced.
- 7.10 The PBAC noted the clinical claims for efficacy of ABRO were based on the results of the composite endpoint of EASI50 and DLQI≥4 response rate, which was not a prespecified outcome in either of the head-to-head trials. The PBAC noted the endpoints in JADE COMPARE were EASI75, as well as IGA response, and in JADE DARE a 4 point or more improvement in the Peak Pruritis Numerical Rating Scale (PP-NRS4) and at least 90% improvement in the EASI score (EASI90). The PBAC agreed with the

submission that the composite endpoint of EASI50 and DLQI \geq 4 was an appropriate outcome for the basis of the clinical claim as it is consistent with the continuing criteria for PBS listings of systemic treatments for whole body severe AD.

- 7.11 The submission chose a timepoint of 16 weeks for assessment of response, which the PBAC considered was reasonable as it aligned with assessment of response in the PBS restrictions for other systemic therapies for severe AD. The PBAC noted that the relative effectiveness of ABRO versus DUPI varies over time due to differences in time to onset of treatment response, and plateauing of treatment response. The PBAC noted that based on EASI75 response (Figure 1), IGA (Figure 2) and also PP-NRS4, a higher proportion of patients responded to ABRO 200 mg by Week 8 compared to ABRO 100 mg and DUPI 300 mg. However, the number of responders to DUPI increased from Week 8 to Week 16, while the number of responders to ABRO 200 mg and 100 mg appeared to plateau.
- 7.12 The PBAC noted there was no statistically significant difference between ABRO 200 mg and DUPI 300 mg with respect to the proportion of patients with severe AD who met the composite endpoint of EASI50 and DLQI \geq 4 response at 16 weeks based on the pooled dataset (RD: 11.5% [95% CI: -0.9, 22.1] in patients with no prior immunomodulatory therapy (IMM) and RD: 1.5% [95% CI: -9.5, 12.5] in patients with prior IMM).⁶ For the comparison between ABRO 100 mg and DUPI 300 mg, the PBAC noted that the results for the composite endpoint suggested that ABRO 100 mg was inferior to DUPI 300 mg (RD=-5.8, 95%CI: -22.8, 11.3 in patients with no prior IMM and RD=-15.7, 95%CI: -45.3, 13.9 in patients with prior IMM). The PBAC noted that interpretation of the results from these comparisons was limited by the post hoc nature of the analyses in small subgroups.
- 7.13 The PBAC noted that the pre-PBAC Response stated that, in the intended population for the 50 mg dose (patients with renal impairment or on strong CYP2C19 inhibitors), the effect of ABRO 50 mg on a patient's AD is likely to be higher than the same dose in patients without moderate to severe renal impairment, or a pharmacokinetic interaction due concomitant intake of strong CYP2C19 inhibitors, but considered that in the absence of clinical evidence it was not possible to make a determination regarding the comparative effectiveness of ABRO 50 mg versus DUPI.
- 7.14 The PBAC noted that based on the evidence presented in the submission, ABRO 200 mg had a differing and potentially poorer safety profile to DUPI, with patients treated with ABRO 200 mg experiencing higher rates of herpes simplex, herpes zoster, folliculitis, nausea, acne, and laboratory abnormalities, as well as numerically higher rates of adverse events overall compared to DUPI. The PBAC noted that rates of conjunctivitis were higher with DUPI. The PBAC noted that long-term comparative

⁶ Note that the results presented in paragraph 7.12 are derived from post-hoc analyses conducted by the applicant and during the evaluation specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plans for JADE COMPARE or JADE DARE. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

safety data is lacking for ABRO and considered that although additional safety data was provided in the PSCR that it was difficult to draw conclusions from the data given the lack of matching.

- 7.15 Overall, the PBAC considered that the clinical claim of inferior comparative effectiveness for ABRO 100 mg once daily versus DUPI 300 mg every 2 weeks was reasonable, with the magnitude of the reduction in response being uncertain. The PBAC considered that the clinical claim of non-inferior safety between ABRO 100 mg and DUPI was reasonably supported by the evidence presented in the submission. The PBAC considered the clinical claim of non-inferior comparative effectiveness for ABRO 200 mg once daily versus DUPI 300 mg every 2 weeks was reasonable. The PBAC considered that the evidence presented in the submission did not adequately support the claim of non-inferior safety between ABRO 200 mg and DUPI, and that overall that ABRO 200 mg appears to have inferior safety to DUPI. The PBAC considered there was a possible minor added benefit for ABRO 200 mg compared with DUPI 300 mg in terms of faster onset of response (as noted in para 7.11). The PBAC considered that this benefit was offset by an increase in treatment related adverse events.
- 7.16 The PBAC noted that the submission presented a CMA of ABRO 200 mg versus DUPI 300 mg and a CUA of ABRO 100 mg versus DUPI 300 mg. The PBAC considered the submission's presentation of a separate CMA and CUA for the two ABRO strengths did not allow for the way that ABRO is likely to be used in clinical practice to be adequately modelled and assessed. The PBAC noted that the pre-PBAC Response stated that an economic model that captured all clinical scenarios would be complex and inherently uncertain given the scenarios would not align with evidence from ABRO clinical trial program. Without data to inform the rates of, and responses to, up and down titration of ABRO, the PBAC agreed with the ESC's advice that the direction of bias would be unclear. On balance, the PBAC considered that pragmatically, the submission's approach to present separate models, while not preferable, was reasonable in this context.
- 7.17 The PBAC noted that the submission presented a CMA over 2 years comparing ABRO 200 mg once daily to DUPI 600 mg subcutaneously as an initial dose and 300 mg every 2 weeks thereafter. The PBAC noted that this approach was consistent with that accepted by the PBAC for the comparison of UPA 15 mg or 30 mg versus DUPI 300 mg every 2 weeks (para 6.53 and 9.1, UPA PSD, July 2021 PBAC meeting and addendum). The Committee noted that the CMA had not accounted for the cost of adverse events or routine monitoring (i.e., complete blood count, and lipids). The PBAC considered the exclusion of AEs was reasonable as patients who could not tolerate the 200 mg dose of ABRO were likely to have their dose reduced to 100 mg, as per the dosing recommendations in the ABRO PI. Overall, the PBAC considered that the cost effectiveness of abrocitinib 200 mg would be acceptable if it were cost-minimised to the lowest cost alternative therapy of DUPI or UPA, using the previously accepted equi-effective doses for DUPI and UPA (para 9.1 UPA PSD, addendum to July 2021 PBAC meeting).

- 7.18 The PBAC considered that the majority of patients would be treated with ABRO 100 mg, given the safety profile of the 200 mg strength (see para 7.14) and the dosing recommendations in the ABRO PI. The Committee noted that given ABRO 100 mg once daily was considered to be inferior to DUPI 300 mg every 2 weeks (para 7.14), it was appropriate for the submission to have presented a CUA. The Committee noted the CUA had a 5-year time horizon, which it considered was reasonable. Based on 16-week response rates of 65.7% for ABRO 100 mg and 71.4% for DUPI 300 mg (in patients without prior use of systemic IMM) the model estimated a base case cost saving per QALY foregone of \$75,000 to < \$95,000.⁷
- 7.19 The Committee considered the magnitude of the difference in response at 16 weeks used in the model to be uncertain given the limitations associated with the post hoc analysis of the composite endpoint of EASI75 and DLQI \geq 4 in the small subset of the overall ITT population in JADE COMPARE with severe AD. The Committee noted that the difference in response with DUPI was greater in the subgroup of patients with prior systemic immunosuppressants (64.3% for ABRO 100 mg versus 80.0% for DUPI 300 mg (see Table 5)) and that the model estimated a lower cost saving per QALY foregone of \$45,000 to < \$55,000 for this subgroup, but considered that this analyses was likely to be unreliable due to the small number of patients included in the subgroup.
- 7.20 The PBAC noted that the ICER for ABRO 100 mg was sensitive to the rate of discontinuation for both therapies after 16 weeks and to the length of time before patients lost response (treatment waning). The Committee noted that there was less of a cost saving (\$45,000 to < \$55,000 per QALY foregone) when the model assumed treatment waning was higher for ABRO 100 mg than for DUPI as presented in Table 13. Further, the PBAC noted that when a lower rate of discontinuation for DUPI was modelled (5% rather than the rate of 6.3% for both DUPI and ABRO 100 mg used in the base case) the cost saving per QALY foregone was also less than in the base case (\$75,000 to < \$95,000 per QALY foregone). The PBAC considered both treatment waning and discontinuation to be uncertain but noted that longer term data for ABRO 100 mg (48 weeks in JADE EXTEND) and DUPI (42 weeks as reported in Table 16, DUPI PSD, March 2020 PBAC meeting) suggest the discontinuation and treatment waning is greater for ABRO than for DUPI. The PBAC considered that the assumption of the same rate of discontinuation and treatment waning after 16 weeks for DUPI and ABRO was not justified and considered that the economic model should apply differential rates as per the multivariate sensitivity analysis in Table 13.
- 7.21 The PBAC recalled that in its consideration of baricitinib for the same indication that it had stated that “the the literature suggests higher willingness to accept (WTA) for

⁷ Note that the results presented in paragraphs 7.18 and 7.19 are derived from post-hoc analyses conducted by the applicant and during the evaluation specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plans for JADE COMPARE or JADE DARE. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

south west quadrant 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)” (para 7.13, baricitinib PSD, July 2021 PBAC meeting) and in that context, the PBAC considered that a cost saving per QALY foregone of \$75,000 to < \$95,000 would be reasonable for ABRO 100 mg. The PBAC considered that ABRO 100 mg would be considered cost-effective at a price that resulted in a cost saving per quality adjusted life year foregone of \$75,000 to < \$95,000 or more compared to DUPI 300 mg based on use of the treatment waning and discontinuation parameters in the CUA sensitivity analyses presented in Table 13 (i.e., multivariate analyses 1+2). The PBAC noted that the resulting price was in general alignment with the clinical evidence, which suggested the dose response between ABRO 100 mg and ABRO 200 mg was not linear (see Table 5 and Figure 1).

- 7.22 The PBAC noted that the submission provided no comparative clinical efficacy or safety data for ABRO 50 mg versus DUPI 300 mg and that according to the ABRO Product Information, the tablets should not be split to obtain a smaller dose. In the absence of clinical evidence, the Committee considered that it would be reasonable for the 50 mg strength of ABRO to be listed at the same price per mg as the 100 mg strength.
- 7.23 The PBAC noted that the submission estimated a net increase in cost to the PBS in the first year of listing due to grandfathering of patients enrolled in a patient familiarisation program. The submission assumed these patients were not captured in the market share approach. The PBAC considered inclusion of grandfather patients in year 1 of the estimates, in addition to the market share values, was not consistent with the assumption of no additional growth in the market, but noted that the net financial impact was minimal. The Committee noted that the listing of ABRO was estimated to be cost saving to the PBS, because listing of ABRO 100 mg would be associated with a lower cost to the PBS than DUPI 300 mg (based on a determination of inferior comparative effectiveness and QALYs foregone), and a price for ABRO 200 mg that would be cost-neutral. The submission assumed no additional growth in the market associated with the introduction of an additional treatment option. The PBAC noted that cost savings would be reduced if sequential use results in any growth in the market.
- 7.24 The PBAC noted the sponsor had indicated they were willing to join the existing Risk Sharing Arrangement for systemic treatments for severe AD. The sponsor did not request any changes to the caps associated with the existing DUPI / UPA RSA. As this listing will provide an alternative to the currently listed agents and the submission assumed no growth in the market from the addition of ABRO, the PBAC considered an increase in the RSA caps is not warranted.
- 7.25 The PBAC recommended that ABRO should not be treated as interchangeable on an individual patient basis with DUPI or UPA.

- 7.26 The PBAC advised that ABRO is not suitable for prescribing by nurse practitioners.
- 7.27 The PBAC recommended that the Early Supply Rule should apply for continuing treatment only.
- 7.28 The PBAC noted that because ABRO is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over dupilumab, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 7.29 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ABROCITINIB					
abrocitinib 200 mg tablet, 28	New	1	28	3	Cibingo
abrocitinib 100 mg tablet, 28	New	1	28	3	Cibingo
abrocitinib 50 mg tablet, 28	New	1	28	3	Cibingo
		Max.qty (packs) multiplier = 1			
		Repeat increases: nil			
Restriction Summary [New] / Treatment of Concept: [New]					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia					
	Administrative Advice: Instructions on the use of the Eczema Area and Severity Index and copyright details can be found here: [insert sponsor-neutral location here or Pfizer's contact details]				
	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: 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.				
	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.				
	Indication: Chronic severe atopic dermatitis				

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	Treatment Phase: Initial treatment with this drug 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 therapy
	AND
	Treatment criteria:
	Must be treated by a dermatologist; OR
	Must be treated by a clinical immunologist
	AND
	Treatment criteria:
	Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).
	AND
	Population criteria:
	Patient must be 18 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.
	Administrative Advice:

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	Instructions on the use of the Physician's Global Assessment (5-point scale) can be obtained from [insert sponsor-neutral location here or Pfizer's contact details]
	Administrative Advice: Where the full number of stated repeat prescriptions was not sought in the original prescription, the balance of the repeats can be sought under this treatment phase listing.
Restriction Summary: [New] / Treatment of Concept: [New]	
	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:
	Patient must not have experienced an inadequate response to this therapy
	AND
	Treatment criteria:
	Must be treated by a dermatologist; OR
	Must be treated by a clinical immunologist
	AND
	Treatment criteria:
	Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).
	AND
	Population criteria:
	Patient must be 18 years of age or older
	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

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	<p>Acceptable scores can be:</p> <p>(a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication.</p> <p>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.</p> <p>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.</p> <p>Document the details of the medium to high potency topical corticosteroids (or calcineurin inhibitors) initially trialled are in the patient's medical records.</p>
Restriction Summary: [New] / Treatment of Concept: [New]	
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Dose change - whole body, or, face/hands
	Administrative Advice: Number of repeats for initiation phase and number of repeats for dose change must not exceed 3 repeats in total for the same initiation phase
	Treatment criteria:
	Patient must not be undergoing each of: (i) commencing treatment through this treatment phase listing, (ii) treatment accessed through this treatment phase on more than 2 consecutive occasions,
	AND
	Treatment criteria:
	Patient must be undergoing existing PBS-subsidised treatment with this therapy where each of the following is true: (i) there is a change in daily dose, (ii) any remaining PBS repeat prescriptions for the strength that the patient is changing from, is marked as 'cancelled',
	AND
	Treatment criteria:
	Must be treated by a dermatologist; OR
	Must be treated by a clinical immunologist
	AND
	Treatment criteria:
	Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).
	AND
	Population criteria:
	Patient must be 18 years of age or older
Restriction Summary: [New] / Treatment of Concept: [New]	
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - treatment of the whole body (Grandfather listing)
	Clinical criteria:

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	Patient must have been receiving treatment with this drug for this PBS indication prior to [1 Month 20XX – insert listing date here]
	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 medicine
	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 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 non-PBS-subsidised therapy with this 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 medicine
	AND
	Clinical criteria:
	Patient must not be experiencing an inadequate response to current non-PBS-subsidised therapy with this medicine
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised systemic medicine for this PBS indication, other than oral corticosteroids
	AND
	Clinical criteria:
	Patient must not have experienced an inadequate response to this medicine in this indication, prior to commencing non-PBS-subsidised therapy with this medicine
	AND
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	AND
	Population criteria:
	Patient must be 18 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:

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	<p>(a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication.</p> <p>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.</p> <p>The name/s of the medium to high potency topical corticosteroids trialled prior to commencing treatment with this medicine must be documented in the patient's medical records.</p>
	<p>Prescribing Instructions: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only.</p>
	<p>Prescribing Instructions: For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>
	<p>Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p>Administrative Advice: Instructions on the use of the Physician's Global Assessment (5-point scale) can be obtained from [insert sponsor-neutral location here or Pfizer's contact details]</p>
Restriction Summary: [New] / Treatment of Concept: [New]	
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - treatment of the face and/or hands (Grandfather listing)
	Clinical criteria:
	Patient must have been receiving treatment with this drug for this PBS indication prior to [1 Month 20XX – insert listing date here]
	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 having commenced non-PBS-subsidised therapy with this 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 having commenced non-PBS-subsidised therapy with this medicine
	AND
	Clinical criteria:
	Patient must have had 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 non-PBS-subsidised therapy with this 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 medicine

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	AND
	Clinical criteria:
	Patient must not be experiencing an inadequate response to current non-PBS-subsidised therapy with this medicine
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised systemic medicine for this PBS indication, other than oral corticosteroids
	AND
	Clinical criteria:
	Patient must not have experienced an inadequate response to this medicine in this indication, prior to commencing non-PBS-subsidised therapy with this medicine
	AND
	Treatment criteria:
	Must be treated by a dermatologist; or
	Must be treated by a clinical immunologist
	AND
	Population criteria:
	Patient must be 18 years of age or older
	<p>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:</p> <ul style="list-style-type: none"> (i) erythema, (ii) oedema/papulation, (iii) excoriation, (iv) lichenification <p>Acceptable scores can be:</p> <ul style="list-style-type: none"> (a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication. <p>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.</p> <p>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.</p> <p>The name/s of the medium to high potency topical corticosteroids trialled prior to commencing treatment with this medicine is/are to be documented in the patient's medical records.</p>
	<p>Prescribing Instructions: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only.</p>
	<p>Prescribing Instructions: For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>
	<p>Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>

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MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ABROCITINIB					
abrocitinib 200 mg tablet, 28	New	1	28	5	Cibingo
abrocitinib 100 mg tablet, 28	New	1	28	5	Cibingo
abrocitinib 50 mg tablet, 28	New	1	28	5	Cibingo
		Max.qty (packs) multiplier = 1			
		Repeat increases: nil			
Restriction Summary [New] / Treatment of Concept: [New]					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia					
	Administrative Advice: Instructions on the use of the Eczema Area and Severity Index and copyright details can be found here: [insert sponsor-neutral location here or Pfizer 's contact details]				
	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: 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.				
	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.				
Indication: Chronic severe atopic dermatitis					
Treatment Phase: Continuing or resuming treatment with this drug of the whole body					
Clinical criteria:					
Patient must have received PBS-subsidised treatment with this therapy 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 maintained an adequate response to their most recent supply of this therapy for this PBS indication if this is any Continuing treatment authority application other than the first; 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					
Treatment criteria:					
Must be treated by a dermatologist; OR					
Must be treated by a clinical immunologist					
AND					
Treatment criteria:					

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	<p>Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).</p> <p>For the purposes of this restriction, an adequate response to treatment 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</p> <p>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.</p> <p>State each of the current EASI and DLQI scores for this authority application.</p>
Restriction Summary: [New] / Treatment of Concept: [New]	
	Indication: Chronic severe atopic dermatitis
	Treatment Phase: Continuing or resuming treatment with this drug of the face and/or hands
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this therapy for the treatment of chronic severe atopic dermatitis affecting the face/hands,
	AND
	Clinical criteria:
	<p>Patient must have achieved an adequate response prior to this first continuing treatment authority application; OR</p> <p>Patient must have maintained an adequate response to their most recent supply of this therapy for this PBS indication if this is any Continuing treatment authority application other than the first; OR</p> <p>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.</p>
	AND
	Treatment criteria:
	Must be treated by a dermatologist; OR
	Must be treated by a clinical immunologist
	Treatment criteria:
	AND
	<p>Patient must be undergoing treatment with this drug as the sole PBS-subsidised therapy with this PBS indication (combination with oral corticosteroids is permitted as these are not listed with the PBS indication: chronic severe atopic dermatitis).</p> <p>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</p>

	<p>(b) An improvement in Dermatology Life Quality Index (DLQI) score of at least 4 points compared to baseline</p> <p>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.</p> <p>Document each qualifying response measure in the patient's medical records for PBS compliance auditing purposes</p>
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These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

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

10 Sponsor's Comment

The sponsor had no comment.