An addendum to this Public Summary Document has been included at the end of the document.

5.02 DEUCRAVACITINIB, Tablet 6 mg, Sotyktu®, Bristol-Myers Squibb Australia Pty Ltd.

1 Purpose of submission

1.1 The Category 1 submission requested an Authority Required (STREAMLINED) listing for deucravacitinib for the treatment of severe chronic plaque psoriasis (CPP) in patients who have not responded to or have a contraindication or demonstrated intolerance to methotrexate.

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus apremilast.

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

Component	Description
Population	Severe chronic plaque psoriasis
Intervention	Deucravacitinib, 6 mg orally once daily
Comparator	Apremilast, 30 mg orally twice daily (after titration)
Outcomes	Co-primary endpoints: sPGA 0/1 and PASI 75 at Week 16 and Week 24[a] Secondary endpoints: sPGA 0, PASI 75, PASI 90, PASI 100, DLQI 0/1 at Week 16
Clinical claim	Compared to apremilast, deucravacitinib is superior in terms of efficacy and non-inferior in terms of safety.

Source: Table 1, p17 of the submission.
DLQI = Dermatology Life Quality Index; PASI = Psoriasis Area Severity Index; sPGA = static Physician Global Assessment.
[a] Table 1 of the submission stated that the co-primary endpoints were measured at 16 and 24 weeks. However, the co-primary outcomes in the included trials were versus placebo at 16 weeks.

2 Background

Registration status

2.1 The submission was made under the TGA/PBAC Parallel Process. At the time of PBAC consideration, the Clinical Evaluation Report(s), Delegate's Overview and Advisory Committee on Medicines (ACM) advice were available.

2.2 The proposed TGA indication for deucravacitinib is "for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy". The TGA Delegate was supportive of approving deucravacitinib for the proposed indication.

3 Requested listing

3.1 The requested listing is presented below. Suggestions and additions proposed by the Secretariat are in italics and suggested deletions are crossed out with strikethrough.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DEUCRAVACITINIB					
Deucravacitinib 6 mg tablet, 28	$1,415.28 published price $[redacted] effective price	1	28	5	Sotyktu®
Category / Program: General Schedule					
Prescriber type: ☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐					
Restriction type: ☒Authority Required (STREAMLINED)					
Episodicity: Chronic					
Severity: Severe					
Condition: Plaque psoriasis					
Indication: Severe chronic plaque psoriasis					
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.*					
Clinical criteria:					
Patient must have not experienced an adequate response after at least 6 weeks of treatment with methotrexate prior to initiating treatment with this drug; OR Patient must have a contraindication to methotrexate according to the Therapeutic Goods Administration (TGA) approved Product Information; OR Patient must have demonstrated severe intolerance of, or toxicity due to, methotrexate.					
AND					
Clinical criteria:					
The condition must have caused significant interference with quality of life.					
AND					
Clinical criteria:					
Patient must not be undergoing concurrent PBS-subsidised treatment for psoriasis with each of: (i) a biological medicine, (ii) ciclosporin; *(iii) apremilast*					
Treatment criteria:					
~~Must be treated by a dermatologist.~~ [b] *Must be treated by a medical practitioner who is either: (i) a dermatologist, (ii) an accredited dermatology registrar in consultation with a dermatologist; OR* *Must be treated by a general practitioner who has been directed to continue treatment (not initiate treatment) by one of the above practitioner types*					
Population criteria:					
Patient must be aged 18 years or older.					

3.2 The submission requested a special pricing arrangement, with a published dispensed price for maximum quantity of $1,415.28. Given the effective price of apremilast was

unknown, the submission proposed an effective price for deucravacitinib based on the published price of apremilast.

3.3 The requested restriction is narrower than the proposed TGA indication, which does not require patients to have not responded or be intolerant to methotrexate, or for the condition to have caused significant interference with quality of life. The requested restriction is different to the population in the underlying clinical trials, which does not include the three clinical criteria listed in the proposed PBS restriction but did include eligibility criteria for body surface area involvement, Psoriasis Area Severity Index (PASI) score and static Physician Global Assessment (sPGA) score.

3.4 In July 2020, the PBAC recommended reimbursement for apremilast to treat CPP based on a cost-minimisation approach with ciclosporin. To ensure the listing was consistent with the eligibility criteria for ciclosporin, the eligible population was required to have severe CPP, with significant interference to quality of life and have not achieved adequate response to prior treatment with methotrexate. The restriction does not include any eligibility criteria based on PASI score, DLQI or body surface area.

3.5 The PBS population proposed by the submission is the same as that of apremilast; limited to patients with severe CPP, with significant interference to quality of life, who have achieved an inadequate response to, or are unable to tolerate, methotrexate.

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

4 Population and disease

4.1 CPP is a chronic immune-mediated skin disorder characterised by the presence of disfiguring, scaling, and erythematous plaques. Patients with CPP experience reduced quality of life, partly because of the discomfort and disability caused by pain and itching, and partly because of the perceived social stigma associated with disfiguration.

4.2 Grading the severity of disease as mild, moderate, and severe can be helpful in guiding management; however, there is some variation in the definition of severe CPP applied by regulatory bodies, reimbursement agencies and clinical practice guidelines.

4.3 Assessment of disease severity incorporates the grading of psoriasis symptoms using PASI score and quality of life using the Dermatology Life Quality Index (DLQI).

4.4 The Australasian College of Dermatologists (ACD) consensus on treatment goals for psoriasis categorises patients in two main groups: mild to moderate and severe. According to the ACD consensus, mild to moderate plaque psoriasis is defined as PASI ≤10 and DLQI ≤10, while severe plaque psoriasis is defined as PASI >10, or PASI ≤10 and DLQI >10.

4.5 The current PBS restrictions limit the use of biologic or targeted synthetic disease modifying anti-rheumatic drugs (herein referred to as 'biologics') to patients with:

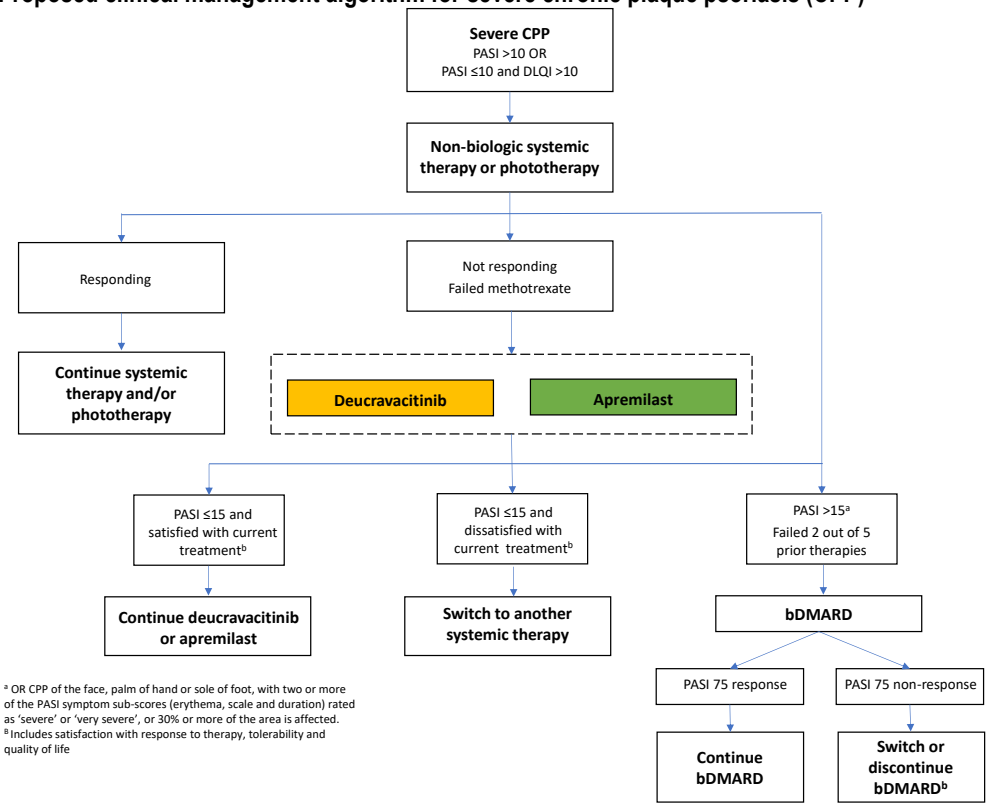
- PASI greater than 15 (this is termed "severe" CPP in the PBS restriction, though terminology relating to mild, moderate, and severe CPP varies between guidelines); or
- CPP of the face, palm of hand or sole of foot, with two or more of the PASI symptom sub-scores (erythema, scale, and duration) rated as 'severe' or 'very severe'; or 30% or more of the area is affected.

4.6 Both the PBS restriction and ACD consensus statement for biologics require that patients have failed or are contraindicated to at least two systemic therapies or phototherapy.

4.7 In April 2018, the PBAC requested a cost-effectiveness review (CER) of biologics for severe CPP under the current PBS restrictions, and to consider the additional PBS population that meet the criteria of a baseline Psoriasis Area and Severity Index (PASI) ≥ 12 to ≤ 15 AND/OR a Dermatology Life Quality Index (DLQI) > 10. At its consideration of the CER in July 2020, the PBAC noted that the incremental cost effectiveness ratio (ICER) for the PASI >15 subgroup was $15,000 - $45,000 per additional quality-adjusted life-year gained (QALY), while the ICER for the PASI ≥12 to ≤ 15 subgroup was $105,000/QALY - $200,000/QALY (paragraph 4.7, biologics for the treatment of severe CPP cost-effectiveness review public summary document (PSD), July 2020 PBAC meeting). The PBAC noted that a price reduction would be required in the PASI ≥ 12 to ≤ 15 subgroup to maintain the same ICER across both populations (paragraph 4.7, biologics for the treatment of severe CPP cost-effectiveness review PSD, July 2020 PBAC meeting).

4.8 The proposed place of deucravacitinib in the clinical management algorithm for severe CPP is after methotrexate and before biologic therapy, as an alternative to apremilast (Figure 1). The ACD consensus statement has not been updated since the PBS listing of apremilast. The potential for sequential use of apremilast and deucravacitinib was not addressed in the submission. The Economic Sub-Committee (ESC) considered the place of deucravacitinib in Australian clinical practice is uncertain.

Figure 1: Proposed clinical management algorithm for severe chronic plaque psoriasis (CPP)



Source: Figure 2, p29 of the submission.
bDMARD = biologic disease modifying anti-rheumatic drug; CPP = chronic plaque psoriasis; PASI = Psoriasis Area Severity Index.

4.9 The ESC noted the sponsor's advisory board stated that predicted use of deucravacitinib will vary depending on the individualised pathway of the patient and the intent of treatment (e.g., treatment to become eligible for biologic therapy, to achieve an efficacy endpoint, preference for oral medication, joint involvement). The ESC considered that, unlike apremilast, deucravacitinib would not be used as a treatment to become eligible for biologic therapy due its longer time to maximum effect.

4.10 The principal pharmacologic action of deucravacitinib is achieved by selectively binding to the regulatory domain of tyrosine kinase 2 (TYK2) and stabilising an inhibitory interaction between the regulatory and the catalytic domains of the enzyme. This inhibits activation of TYK2 and its downstream functions in cells, including the signalling of cytokines involved in inflammatory and immune responses. At therapeutic doses, deucravacitinib blocks TYK2 without inhibiting Janus kinase (JAK) 1, JAK2, or JAK3, thus potentially avoiding adverse events associated with JAK inhibitors (tofacitinib, upadacitinib, and baricitinib). The mechanism of action for deucravacitinib is different to apremilast, which is a PDE-4 inhibitor. The ESC noted the TGA Delegate Overview had stated that TYK2 is a member of the JAK family of non-receptor tyrosine kinases and that other small molecule drugs that inhibit the activity

of JAKs have been implicated in increased reports of major cardiac adverse cardiac events, malignancy, mortality, thromboembolic events, diverticulitis and gastrointestinal haemorrhage in several patient populations. The ACM was of the view that although the mechanism of action seemed to be different to other available JAK inhibitors, there is no certainty of long-term safety yet. On that basis, the ACM recommended that, if approved, cautionary statements be included in the PI to the effect that although causality has not been firmly established, the data are not yet available to give certainty that deucravacitinib will be safter than other JAK-STAT agents approved for this condition.

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

5 Comparator

5.1 The submission nominated apremilast as the main comparator. The main arguments provided in support of this nomination were:

- Both are oral therapies positioned in patients with severe CPP.
- Apremilast is the therapy most likely to be replaced by deucravacitinib.

5.2 The submission noted that ciclosporin is also used in patients with severe CPP who have not responded to methotrexate but expected that its use would have largely been replaced by apremilast. Further, the submission noted that since apremilast was listed based on a cost-minimisation approach with ciclosporin a comparison between deucravacitinib and ciclosporin would be redundant.

5.3 Patients with severe CPP are also eligible for phototherapy. Phototherapy for severe CPP is listed on the MBS and could be considered a relevant alternative therapy for deucravacitinib. No information was provided in the submission to inform a comparison of deucravacitinib and phototherapy.

5.4 The evaluation considered biologic therapies for severe CPP may be considered a more appropriate main comparator for deucravacitinib because:

- Patients with chronic plaque psoriasis, PASI >15, and who have failed two of phototherapy, methotrexate, ciclosporin, acitretin, and apremilast are eligible for biologic therapies. The proposed PBS population for deucravacitinib and biologic therapies overlap.
- A 2020 meta-analysis comparing biologics and oral treatments for plaque psoriasis showed apremilast was outperformed by biologics, many of which are PBS listed.[1] If deucravacitinib demonstrates superior effectiveness to apremilast, more

[1] Armstrong et. al., (2020), Comparison of Biologics and Oral Treatments for Plaque Psoriasis: A Meta-Analysis, JAMA Dermatology, 156(3):258-269. https://jamanetwork.com/journals/jamadermatology/fullarticle/2759772

patients currently eligible for biologics may opt for this oral treatment rather than for biologics.

5.5 If biologic therapies are not considered to be a more appropriate main comparator, they are likely to be used as subsequent therapies in eligible patients. This was not captured in the trial or financial estimates but was assumed in the economic analysis.

5.6 The Pre-Sub-Committee Response (PSCR) acknowledged the proposed deucravacitinib PBS indication theoretically overlaps with the PBS listings for biologics (in patients with PASI>15), however argued that based on clinician feedback there is unlikely to be substitution of biologics by deucravacitinib in clinical practice. The PSCR also argued the clinical profile associated with deucravacitinib favours use prior to biologics, and patients with a strong aversion to needles are likely to already be using apremilast as an oral alternative, making apremilast the appropriate comparator in these patients, and patients currently treated with biologics are likely to continue treatment with biologics.

5.7 The ESC considered that, whilst the proposed positioning of deucravacitinib was the same as apremilast, given the overlap with the population who may be considered for biologics, biologic therapies should also be considered comparators. The Pre-PBAC Response stated that while there may be a subgroup of patients in the proposed listing who have access to biologics, acknowledged that deucravacitinib may not be as efficacious as some biologics. The Sponsor also stated that previous PBAC considerations of apremilast, in which theoretically a similar overlap exists, did not include any advice that biologics should be considered a comparator.

5.8 The PBAC considered the place in therapy for deucravacitinib and most appropriate primary comparator(s) remained uncertain and further considered expert dermatologists' clinical advice would be informative to resolve this issue.

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 health care professionals (3) and organisations (1) via the Consumer Comments facility on the PBS website. The comments from health professionals noted patients with chronic plaque psoriasis often have poor quality of life due to their symptoms often being uncontrolled by topical treatments, and noted deucravacitinib is considered an option for this group to manage their symptoms and improve quality of life. The comments from health care professionals also noted while deucravacitinib is believed to be less efficient than

some treatments for the management of severe plaque psoriasis (i.e. some biologics), deucravacitinib is considered a safe and effective oral alternative to injectable therapies.

6.3 The PBAC also noted the advice from Creaky Joints Australia, which noted the impact of plaque psoriasis on patients' lives and shared patient experiences of living with the condition. The experiences highlighted the physical and mental impacts of plaque psoriasis, including how the visible aspect of psoriasis leads to anxiety, depression and body image problems. The input also described the lack of effective treatment options for patients who cannot use biologics and noted some of the currently available systemic non-biologic treatment options have maximum safe durations of therapy, highlighting the need for an effective alternative to currently available biologic therapies, which may also have cost benefits to the PBS through delaying (or prevent the need in some cases) biologic therapy.

Clinical trials

6.4 The submission was based on two randomised trials comparing deucravacitinib (6 mg once daily) versus placebo and apremilast (30 mg twice daily) in patients with moderate-to-severe plaque psoriasis: POETYK 1 (n = 666) and POETYK 2 (n = 1,020).

6.5 The eligibility criteria were identical across the POETYK 1 and POETYK 2 trials.

6.6 Patients could have received, but were not required to receive, prior treatment with systemic non-biologics, immunosuppressants, phototherapy or biologic therapy. However, patients could not have received systemic non-biologics, immunosuppressants or phototherapy within four weeks of Day 1 of the study or biologics within 3 to 6 months (depending on mechanism of action) of Day 1 of the study. As a result:

- The percentage of patients with prior systemic therapy use (biologic or non-biologic) ranged from 60.6% to 64.9% in the POETYK 1 trial and 53.6% and 55.1% in the POETYK 2 trial.
- The percentage of all patients receiving prior biologic therapy ranged from 38.0% to 39.2% in the POETYK 1 trial and 31.1% and 32.5% in the POETYK 2 trial (p82 of the POETYK 1 CSR, p96 of the POETYK 2 CSR).

6.7 Residual biologic therapy may confound the treatment effect across all arms in the POETYK 1 and POETYK 2 trials.

6.8 The percentage of patients with prior systemic therapy in both trials is also inconsistent with the proposed PBS restriction, which requires patients to have failed methotrexate before receiving deucravacitinib. In an Australian setting, 100% of patients will have had prior systemic therapy (with methotrexate, unless contraindicated). It is also inconsistent with the proposed clinical management algorithm, which positions deucravacitinib before treatment with biologics.

6.9 The submission presented a meta-analysis of the POETYK 1 and POETYK 2 trials. The submission claimed that the baseline demographic disease, and prior therapy information were similar enough to warrant meta-analysis of their results. There were slight differences in race, duration of disease, location of psoriasis, and prior systemic therapy across the trials. However, the trials appear similar enough for a meta-analysis to be appropriate.

6.10 The submission presented two subgroup analyses that attempted to address potential applicability issues between the POETYK 1 and POETYK 2 trials and the intended Australian population:

- Patients with high PASI baseline score (defined as PASI > 15) and patients with low PASI baseline score (defined PASI ≤ 15); and
- Patients with prior non-biologic therapy use at baseline and patients with no prior non-biologic therapy use at baseline.

6.11 The treatment algorithm presented in the submission (Figure 1) indicated that patients would receive systemic non-biologic therapies (including deucravacitinib) before biologic therapy. Patients in the POETYK 1 and POETYK 2 trials who have already received biologic therapies may not be representative of the Australian population.

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

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
POETYK 1 (IM011046) NCT03624127	A Multi-Center, Randomized, Double-Blind, Placebo- and Active Comparator-Controlled Phase 3 Study to Evaluate the Efficacy and Safety of BMS-986165 in Subjects with Moderate-to Severe Plaque Psoriasis Armstrong A, Gooderham M, Warren RB et al. Efficacy and safety of deucravacitinib, an oral, selective tyrosine kinase 2 (TYK2) inhibitor, compared with placebo and apremilast in moderate to severe plaque psoriasis: Results from the phase 3 POETYK PSO-1 study	CSR, August 2021 Annals of the Rheumatic Diseases 2021; 80(SUPPL 1): 795-796.
POETYK 2 (IM011047) NCT03611751	A Multi-Center, Randomized, Double-Blind, Placebo- and Active Comparator-Controlled Phase 3 Study with Randomized Withdrawal and Retreatment to Evaluate the Efficacy and Safety of BMS-986165 in Subjects with Moderate-to-Severe Plaque Psoriasis	CSR, August 2021

Source: Table 14, p38 of the submission.
CSR = clinical study report.

6.13 The key features of the direct randomised trials are summarised in Table 3. The economic analysis used pooled individual patient data from the POETYK trials for PASI 75, 90, and 100 response and proportion of patients with an absolute PASI score >15 at weeks 8, 16, and 24.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
Deucravacitinib versus apremilast and versus placebo						
POETYK 1	666	MC, R, DB 52 wks.	Low	Aged ≥ 18 years with moderate-to-severe plaque psoriasis, defined as PASI ≥12 AND sPGA ≥3 AND BSA involvement ≥10%.	Co-1º: sPGA 0/1 response [a], PASI 75 response [a] 2º: sPGA 0/1 response [b], PASI 75 response [b], sPGA 0 response [a, b], PASI 90 response [a, b], PASI 100 response [a, b], DLQI 0/1 score [a, b].	Used – IPD
POETYK 2	1,020	MC, R, DB 52 wks.	Low	Aged ≥ 18 years with moderate-to-severe plaque psoriasis, defined as PASI ≥12 AND sPGA ≥3 AND BSA involvement ≥10%.	Co-1º: sPGA 0/1 response [a], PASI 75 response [a] 2º: sPGA 0/1 response [c], PASI 75 response [c], sPGA 0 response [a, c], PASI 90 response [a, c], PASI 100 response [a, c], DLQI 0/1 score [a, c].	Used – IPD
Meta-analysis	1,686	Included POETYK 1 and POETYK 2; subgroup analysis using baseline PASI score assessed PASI 75, 90 and 100 response; subgroup analysis using prior non-biologic systemic therapy assessed PASI 75 response.				Not used

Source: Tables 15, 18 & 19, pp39, 45 & 49-50 of the submission. Table 3.5-1, pp38-41 of the POETYK 1 CSR, Table 3.5-1, pp46-49 of the POETYK 2 CSR.

Co-1º = co-primary; 2º = secondary; BSA = body surface area; DB = double blind; DLQI = dermatology life quality index; IPD = individual patient data; MC = multi-centre; PASI = Psoriasis Area and Severity Index; R = randomised; sPGA = static Physician's Global Assessment; wks. = weeks.

[a] Versus placebo at week 16.

[b] Versus apremilast at weeks 16, 24, and 52.

[c] Versus apremilast at weeks 16 & 24.

6.14 The co-primary efficacy endpoints in both trials compared deucravacitinib with placebo, not apremilast. The comparative effectiveness of deucravacitinib and apremilast was based on secondary outcomes in the POETYK 1 and POETYK 2 trials.

6.15 The sPGA score is a 5-point scale of an average assessment of all psoriasis lesions based on erythema, scaling, and induration. The sPGA score determines psoriasis severity by allocating patents to categories: clear (0), almost clear (1), mild (2), moderate (3), or severe (4). An sPGA 0/1 response is defined as an sPGA score of 0 or 1 in subjects with ≥ 2-point improvement from baseline.

6.16 PASI refers to the average redness, thickness, and scaliness of psoriasis skin lesions, graded on a scale from 0-4 and weighted by the area of involvement. The PASI measure produces a score from 0-72, with higher scores indicating greater disease severity. PASI 75 refers to the proportion of patients who experienced at least a 75% improvement in PASI score since baseline, which allows the assessment of patients' response to treatment.

6.17 The study design for both trials included treatment switching after week 16, some of which was based on treatment response. The POETYK 2 trial also included treatment withdrawal after week 24 in some treatment arms. Although the trials had a duration

of 52 weeks, the comparative evidence is limited to 16 weeks versus placebo and 24 weeks versus apremilast. The comparative evidence presented is short relative to the chronic nature of severe CPP. However, the duration of treatment/efficacy assessment is similar to that presented for apremilast in severe CPP (paragraph 6.5, apremilast PSD, March 2015 PBAC meeting; paragraph 6.7, apremilast PSD, November 2016 PBAC meeting, paragraph 6.5, apremilast, PSD, November 2017 PBAC meeting).

6.18 PASI response is a clinically relevant outcome.[2] The PBAC relied on PASI 75 response for the assessment of apremilast in severe CPP (paragraph 6.7, apremilast PSD, March 2015 PBAC meeting; paragraph 6.9, apremilast PSD, November 2016 PBAC meeting, paragraph 6.6, apremilast PSD, November 2017 PBAC meeting).

Comparative effectiveness

Whole trial analysis and meta-analysis

6.19 The results comparing key outcomes for deucravacitinib and apremilast are summarised in Table 4.

[2] Australian College of Dermatologists (2017) Consensus statement: Treatment goals for psoriasis, https://www.dermcoll.edu.au/wp-content/uploads/ACD-Consensus-Statement-Treatment-goals-for-psoriasis-March-2017.pdf

Table 4: Whole trial and meta-analysis results: deucravacitinib and apremilast

Time point	Trial ID	Deucravacitinib n/N (%)	Apremilast n/N (%)	Odds Ratio (95% CI)	Risk difference (95% CI)
sPGA 0/1					
Wk. 16	POETYK 1	178/332 (53.6)	54/168 (32.1)	**2.44 (1.65, 3.60)**	**0.21 (0.12, 0.30)**
	POETYK 2	253/511 (49.5)	86/254 (33.9)	**1.92 (1.40, 2.62)**	**0.16 (0.08, 0.23)**
	Meta-analysis	431/843 (51.1)	140/422 (33.2)	**2.11 (1.65, 2.69) p < 0.00001**	**0.18 (0.12, 0.24) p < 0.00001**
		Heterogeneity (I^2); p-value		0%; 0.34	0%; 0.32
Wk. 24	POETYK 1	195/332 (58.7)	52/168 (31.0)	**3.18 (2.14, 4.71)**	**0.28 (0.19, 0.37)**
	POETYK 2	251/504 (49.8)	75/254 (29.5)	**2.37 (1.72, 3.26)**	**0.20 (0.13, 0.27)**
	Meta-analysis	446/836(53.3)	127/422 (30.1)	**2.68 (2.02, 3.56) p < 0.00001**	**0.24 (0.16, 0.31) p < 0.00001**
		Heterogeneity (I^2); p-value		22%; 0.26	41%; 0.19
PASI 75					
Wk. 16	POETYK 1	194/332 (58.4)	59/168 (35.1)	**2.60 (1.77, 3.82)**	**0.23 (0.14, 0.32)**
	POETYK 2	271/511 (53.0)	101/254 (39.8)	**1.71 (1.26, 2.32)**	**0.13 (0.06, 0.21)**
	Meta-analysis	465/843 (55.2)	160/422 (37.9)	**2.07 (1.38, 3.12) p = 0.0005**	**0.18 (0.08, 0.28) p = 0.0003**
		Heterogeneity (I^2); p-value		64%; 0.10	65%; 0.09
Wk. 24	POETYK 1	230/332 (69.3)	64/168 (38.1)	**3.66 (2.48, 5.41)**	**0.31 (0.22, 0.40)**
	POETYK 2	296/504 (58.7)	96/254 (37.8)	**2.34 (1.72, 3.19)**	**0.21 (0.14, 0.28)**
	Meta-analysis	526/836(62.9)	160/422 (37.9)	**2.88 (1.86, 4.46) p < 0.00001**	**0.26 (0.16, 0.36) p < 0.00001**
		Heterogeneity (I^2); p-value		68%; 0.08	67%; 0.08
DLQI 0/1 [a]					
Wk. 16	POETYK 1	132/322 (41.0)	46/161 (28.6)	**1.74 (1.16, 2.61)**	**0.12 (0.04, 0.21)**
	POETYK 2	186/495 (37.6)	57/247 (23.1)	**2.01 (1.42, 2.84)**	**0.14 (0.08, 0.21)**
	Meta-analysis	318/817 (38.9)	103/408 (25.2)	**1.89 (1.45, 2.46) p < 0.00001**	**0.14 (0.08, 0.19) p < 0.00001**
		Heterogeneity (I^2); p-value		0%; 0.60	0%; 0.71

Source: Tables 27-30, 34 & 45, pp64-67, 71 & 101 of the submission.

CI = confidence interval; DLQI = dermatology life quality index; n = number of participants with event; N = total participants in group; PASI = Psoriasis Area and Severity Index; sPGA = static Physician's Global Assessment, wk. = week. **Bold** indicates statistically significant results.

[a] Non-responder imputation was used for binary endpoints for subjects who had discontinued treatment or study prior to timepoint of comparison or had missing endpoint data at timepoint of comparison.

6.20 A statistically significantly greater proportion of patients treated with deucravacitinib compared to apremilast achieved an sPGA score of 0 or 1 at week 16 in both trials (POETYK 1: odds ratio (OR) [95% CI] =2.44 [1.65, 3.60]; POETYK 2: OR [95% CI] = 1.92 [1.40, 2.62]).

6.21 Similarly, a statistically significantly greater proportion of patients treated with deucravacitinib compared to apremilast achieved a sPGA score of 0 or 1 at week 24 in both trials (POETYK 1: OR [95% CI] = 3.18 [2.14, 4.71]; POETYK 2: OR [95% CI] = 2.37 [1.72, 3.26]).

6.22 A statistically significantly greater proportion of patients treated with deucravacitinib compared to apremilast achieved a PASI 75 score at week 16 in both trials (POETYK 1: OR [95% CI] = 2.60 [1.77, 3.82]; POETYK 2: OR [95% CI] = 1.71 [1.26, 2.32]).

6.23 When meta-analysed, the proportion of patients achieving PASI 75 at week 16 was 55.2% in the deucravacitinib arm and 37.9% in the apremilast arm. This difference was statistically significant in favour of deucravacitinib with an OR [95% CI] of 2.07 [1.38, 3.12].

6.24 A statistically significantly greater proportion of patients treated with deucravacitinib compared to apremilast achieved a PASI 75 score at week 24 in both trials (POETYK 1: OR [95% CI] = 3.66 [2.48, 5.41]; POETYK 2: OR [95% CI] = 2.34 [1.72, 3.19]).

6.25 When meta-analysed, the proportion of patients achieving PASI 75 at week 24 was 62.9% in the deucravacitinib arm and 37.9% in the apremilast arm. This difference was statistically significant in favour of deucravacitinib with an OR [95% CI] of 2.88 [1.86, 4.46].

6.26 A statistically significantly greater proportion of patients treated with deucravacitinib compared to apremilast achieved a DLQI score of 0 or 1 at week 16 in both trials (POETYK 1: OR [95% CI] =1.74 [1.16, 2.61]; POETYK 2: OR [95% CI] = 2.01 [1.42, 2.84]).

6.27 The magnitude of the treatment effect (OR and risk difference) differed between the POETYK 1 and POETYK 2 trials for each outcome; however, the tests for heterogeneity were non-significant (Table 4).

Subgroup analyses

6.28 Subgroup analyses comparing PASI 75 response for deucravacitinib and apremilast at 16 weeks are summarised in Table 5.

Table 5: Results of subgroup analyses: PASI 75 at week 16, deucravacitinib and apremilast

Population	Trial ID	Deucravacitinib n/N (%)	Apremilast n/N (%)	OR (95% CI)	RD (95% CI)
Subgroup analysis 1: PASI baseline score (high versus low)					
High baseline PASI score (PASI >15) [a]	POETYK 1	157/258 (60.9)	47/122 (38.5)	2.48 (1.59, 3.86)	0.22 (0.12, 0.33)
	POETYK 2	212/384 (55.2)	80/202 (39.6)	1.88 (1.33, 2.66)	0.16 (0.07, 0.24)
	Meta-analysis of High PASI group	369/642 (57.5)	127/324 (39.2)	2.09 (1.59, 2.74)	0.18 (0.12, 0.25)
Low baseline PASI score (PASI ≤15) [a]	POETYK 1	37/74 (50.0)	12/46 (26.1)	2.83 (1.27, 6.31)	0.24 (0.07, 0.41)
	POETYK 2	59/127 (46.5)	21/52 (40.4)	1.28 (0.67, 2.46)	0.06 (-0.10, 0.22)
	Meta-analysis of Low PASI group	96/201 (47.8)	33/98 (33.7)	1.84 (0.85, 3.99)	0.15 (-0.03, 0.32)
Test for subgroup differences, p-value		–	–	0.76 Based on OR = 0.76 Based on RD = 0.71	
Subgroup analysis 2: prior non-biologic therapy (yes versus no)					
Prior non-biologic therapy [a]	POETYK 1	46/70 (65.7)	18/43 (41.9)	2.66 (1.22, 5.82)	0.24 (0.05, 0.42)
	POETYK 2	62/109 (56.9)	27/61 (44.3)	1.66 (0.88, 3.12)	0.13 (-0.03, 0.28)
	Meta-analysis of prior non-biologics group	108/179 (60.3)	45/104 (43.3)	2.00 (1.22, 3.27)	0.17 (0.05, 0.29)
No prior non-biologic therapy [a]	POETYK 1	148/262 (56.5)	41/125 (32.8)	2.66 (1.70, 4.16)	0.24 (0.14, 0.34)
	POETYK 2	209/402 (52.0)	74/193 (38.3)	1.74 (1.23, 2.47)	0.14 (0.05, 0.22)
	Meta-analysis of no prior non-biologics group	357/664 (53.8)	115/318 (36.2)	2.10 (1.39, 3.18)	0.18 (0.08, 0.28)
Test for subgroup differences, p-value		–	–	0.88 Based on OR = 0.88 Based on RD = 0.90	

Source: Tables 41 & 42, pp98 & 99 of the submission; Attachment 3 of the submission.

CI = confidence interval; n = number of participants with event; N = total participants in group; NR =not reported; OR = odds ratio; PASI = Psoriasis Area and Severity Index; RD = risk difference.

[a] The number of patients experiencing events in each subgroup was supported by IPD not provided with the submission and therefore could not be verified.

6.29 The magnitude of the treatment effect (OR) in favour of deucravacitinib relative to apremilast was larger in the high PASI subgroup compared to the low PASI subgroup for the proportion of patients achieving PASI 75. Notwithstanding, the test for subgroup differences for PASI 75 was not statistically significant (p=0.76).

6.30 The magnitude of the treatment effect in favour of deucravacitinib relative to apremilast was similar in the prior non-biologic therapy subgroup compared to the subgroup with no prior non-biologic therapy for the proportion of patients achieving

PASI 75. The test for subgroup differences for PASI 75 was not statistically significant (p=0.88).

6.31 The subgroup analyses suggest that the treatment effect observed for deucravacitinib versus apremilast is unlikely to be affected by baseline PASI score (>15 versus ≤15) or prior treatment with systemic non-biologic therapy.

6.32 As with the whole trial analysis, the magnitude of the treatment effect (OR and risk difference) differed between subgroups in the POETYK 1 and POETYK 2 trials for each outcome; however, the tests for heterogeneity were non-significant.

6.33 Patients in the POETYK 1 and POETYK 2 trials who have already received biologic therapies may not be representative of the Australian population. The evaluation noted a subgroup analysis comparing patients with and without prior biologic therapy would be informative to assess whether there is a differential effect based on prior biologic therapy.

6.34 The PSCR presented the results of an additional subgroup analysis on PASI 75 at week 16 considering patients with prior methotrexate but no prior biologic use, which the Sponsor considered to include patients most likely to use deucravacitinib in clinical practice. The PSCR noted these subgroup analyses of the pooled POETYK trial data show similar treatment effects for the prior methotrexate but no prior biologic use subgroup (OR = 1.90, 95%CI: 0.98, 3.66, p=0.06) and the complement subgroup (OR = 2.03, 95%CI: 1.57, 2.63, p<0.0001) and noted these results were similar to that observed in Warren 2021[3].

6.35 The PSCR also argued the 6-month washout period for patients who had received prior biologics would limit the potential impact of residual biologic therapy effects and further argued subgroup analyses from the POETYK trials demonstrate that the use of prior biologics was balanced across treatment arms and deucravacitinib maintains its benefit over apremilast in the subgroups most applicable to the proposed positioning (noted in the above paragraph).

6.36 The ESC noted the subgroup analyses by prior biologic use requested in the evaluation were not specifically provided in the PSCR but the Warren 2021 data provided alongside the PSCR included some relevant subgroup analyses. For the comparison of deucravacitinib vs apremilast, the ESC noted the treatment effect appeared to be larger in patients that had received prior biologic therapy but the data had not been fully evaluated.

[3] Warren , R., Armstrong , A., Gooderham, M., Strober , B., Thaci, D., Imafuku, S., Sofen, H., Spelman, L., Korman, N., Zheng, M., Colston, E., Throup , J., Kundu, S., Kisa, R., Banerjee, S., & Blauvelt, A. . (2022). Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, in Moderate to Severe Plaque Psoriasis: 52-Week Efficacy Results From the Phase 3 POETYK PSO-1 and PSO-2 Trials. SKIN The Journal of Cutaneous Medicine, 6(2), s4. https://doi.org/10.25251/skin.6.supp.4

6.37 Furthermore, given its view that biologics are also relevant comparators, the ESC considered it would be informative to assess the comparative effectiveness of deucravacitinib and alternative biologic therapies to assist in assessing the cost-effectiveness of deucravacitinib in the broader treatment landscape for severe CPP. The ESC noted these additional analyses would likely require evaluation if the PBAC were to assess the comparative effectiveness and cost effectiveness of deucravacitinib and PBS listed biologic therapies for severe CPP. The Pre-PBAC Response argued that as apremilast was the appropriate primary comparator and the proposed place in therapy was the most realistic, the clinical evidence and economic model were sufficient to assess the cost-effectiveness of deucravacitinib in CPP. The PBAC agreed with the ESC and considered biologics may be considered relevant comparators, however given the place in therapy was unclear, considered it was appropriate to seek expert clinical advice to consider these issues further.

Patient reported outcomes – Quality of life outcomes (utilities)

6.38 Table 6 shows the trial-based utilities reported in the POETYK 1 and POETYK 2 trials used as a sensitivity analysis in the economic evaluation.

Table 6: EQ-5D utility value summary statistics (baseline) from the POETYK 1 and POETYK 2 trials, PRO analysis set[a]

	Deucravacitinib		Apremilast	
	n	Mean (SD)	n	Mean (SD)
POETYK 1	323	0.814 (0.1596)	158	0.793 (0.2056)
POETYK 2	482	0.840 (0.1769)	243	0.822 (0.1773)
Pooled	805	0.830 (0.1706)	401	0.810 (0.1892)

Source: Table 78, p149 of the submission

SD = standard deviation; n = number of participants reporting data; PRO = patient reported outcomes.

[a] The PRO analysis set (PAS) is the subset of the full analysis set who completed at least one item at baseline and at least one item post baseline for the respective PRO instrument.

Comparative harms

6.39 The results of key safety outcomes for deucravacitinib and apremilast at week 16 in the POETYK 1 and POETYK 2 trials are summarised in the table below.

Table 7: Summary safety outcomes: deucravacitinib and apremilast, week 16

Trial ID	Deucravacitinib n with event/N (%)	Apremilast n with event/N (%)	OR (95% CI)	RD (95% CI)
POETYK 1				
Deaths	0/332 (0.0)	0/168 (0.0)	NE	0.00 (-0.01, 0.01)
SAEs	7/332 (2.1)	4/168 (2.4)	0.88 (0.25, 3.06)	-0.00 (-0.03, 0.02)
Related SAEs	1/332 (0.3)	2/168 (1.2)	0.25 (0.02, 2.79)	-0.01 (-0.03, 0.01)
AEs	176/332 (53.0)	93/168 (55.4)	0.91 (0.63, 1.32)	-0.02 (-0.12, 0.07)
Related AEs	65/332 (19.6)	36/168 (21.4)	0.89 (0.56, 1.41)	-0.02 (-0.09, 0.06)
Discontinued due to AEs	6/332 (1.8)	10/168 (6.0)	0.29 (0.10, 0.81)	-0.04 (-0.08, -0.01)
POETYK 2				
Deaths	1/510 (0.2)	1/254 (0.4)	0.50 (0.03, 7.98)	-0.00 (-0.01, 0.01)
SAEs	8/510 (1.6)	1/254 (0.4)	4.03 (0.50, 32.41)	0.01 (0.00, 0.03)
Related SAEs	1/510 (0.2)	0/254 (0.0)	1.50 (0.06, 36.92)	0.00 (-0.01, 0.01)
AEs	293/510 (57.5)	150/254 (59.1)	0.94 (0.69, 1.27)	-0.02 (-0.09, 0.06)
Related AEs	99/510 (19.4)	73/254 (28.7)	0.60 (0.42, 0.85)	-0.09 (-0.16, -0.03)
Discontinued due to AEs	14/510 (2.7)	12/254 (4.7)	0.57 (0.26, 1.25)	-0.02 (-0.05, 0.01)
Meta-analysis				
Deaths	1/842 (0.1)	1/422 (0.2)	0.50 (0.03, 7.98)	-0.00 (-0.01, 0.01)
SAEs	15/842 (1.8)	5/422 (1.2)	1.50 (0.35, 6.40)	0.01 (-0.00, 0.02)
Related SAEs	2/842 (0.2)	2/422 (0.5)	0.48 (0.07, 3.28)	-0.00 (-0.01, 0.01)
AEs	469/842 (55.7)	243/422 (57.6)	0.93 (0.73, 1.17)	-0.02 (-0.08, 0.04)
Related AEs	164/842 (19.5)	109/422 (25.8)	0.71 (0.48, 1.05)	-0.06 (-0.13, 0.01)
Discontinued due to AEs	20/842 (2.4)	22/422 (5.2)	0.44 (0.23, 0.84)	-0.03 (-0.05, -0.00)

Source: Table 36, p77 of the submission.

CI = confidence interval; n = number of participants reporting data; N = total participants in group; NE = not estimable; OR = odds ratio; RD = risk difference.

6.40 Two important potential safety risks were identified in the submission: serious infections and malignancies. A meta-analysis of infection events at week 16 across both trials produced an OR [95% CI] of 2.06 [0.34, 12.52] (favouring apremilast), although the difference was not statistically significant (p=0.43). A meta-analysis of malignancy events across the POETYK trials at week 16 produced an OR [95% CI] of 0.37 [0.03, 5.41] (favouring deucravacitinib), although the difference was not statistically significant (p = 0.47).

6.41 In addition, two important potential safety risks are listed in the apremilast PI: depression, and diarrhoea, nausea and vomiting. A meta-analysis of the POETYK trials concluded that 12.0% of deucravacitinib patients and 25.8% of apremilast patients experienced a gastrointestinal disorder at week 16. A meta-analysis produced an OR [95% CI] of 0.40 [0.28, 0.56], favouring deucravacitinib (p<0.00001). A meta-analysis of the POETYK trials for depression at week 16 conducted during the evaluation found no difference between deucravacitinib and apremilast (OR = 3.00, 95% CI: 0.36, 25.12; p = 0.11).

6.42 Overall, the adverse event profile of deucravacitinib was similar to apremilast in the POETYK 1 and POETYK 2 trials. However, the trial duration may not be long enough to capture increased rates of long-term issues such as infection, malignancy, and

depression. There was no long-term follow-up safety data provided with the submission.

Benefits/harms

6.43 A summary of the comparative benefits and harms for deucravacitinib versus apremilast is presented in Table 8.

Table 8: Summary of comparative benefits and harms for deucravacitinib and apremilast

Trial	DEUC n/N	APM n/N	Event rate/100 patients/16 weeks*		RD (95% CI)
			DEUC	APM	
Benefits					
sPGA 0/1 score					
Meta-analysis	431/843	140/422	51.1	33.2	**0.18 (0.12, 0.24)**
PASI 75 response					
Meta-analysis	465/843	160/422	55.1	37.9	**0.18 (0.08, 0.28)**
DLQI 0/1 score [a]					
Meta-analysis	318/817	103/408	38.9	25.2	**0.14 (0.08, 0.19)**
Harms					
	DEUC n/N	**APM n/N**	**Event rate/100 patients/16 weeks***		**RD (95% CI)**
			DEUC	**APM**	
Infection					
Meta-analysis	6/842	1/422	0.7	0.2	0.00 (-0.00, 0.01)
Gastrointestinal disorders					
Meta-analysis	101/842	109/422	12.0	25.8	-0.14 (-0.19, -0.09)
Depression					
Meta-analysis	5/842	0/422	0.6	0.0	0.01 (-0.00, 0.01)

Source: Tables 27, 28, 34 & 39, pp64, 65, 71 & 87-90 of the submission.

APM = apremilast; DEUC = deucravacitinib; DLQI = dermatology life quality index; HR = hazard ratio; PASI, Psoriasis Area and Severity Index; RD = risk difference; RR = risk ratio; sPGA, static Physician's Global Assessment. **Bold** indicates statistically significant results.

***** Duration of follow-up: 52 weeks in the POETYK 1 and POETYK 2 trials, event rates calculated based on results at 16 weeks.

[a] Non-responder imputation was used for binary endpoints for subjects who had discontinued treatment or study prior to timepoint of comparison or had missing endpoint data at timepoint of comparison.

6.44 On the basis of direct evidence presented by the submission, for every 100 patients treated with deucravacitinib in comparison with apremilast over a 16-week (4 month) period:

- Approximately 18 additional patients would have a PASI 75 response.
- Approximately 18 additional patients would have an sPGA score of zero or one.
- Approximately 14 additional patients would have a DLQI score of zero or one.
- Approximately 14 fewer patients would experience gastrointestinal disorders (such as nausea, vomiting, and diarrhoea)

Clinical claim

6.45 The submission described deucravacitinib as superior in terms of efficacy compared with apremilast based on sPGA 0/1 score and PASI 75 at week 16. The ESC considered

the claim was reasonable. However, the ESC also considered it would be informative to assess the comparative effectiveness of deucravacitinib and PBS-listed biologics for severe CPP (as discussed in paragraph 6.37 above).

6.46 However, in the POETYK 1 and POETYK 2 trials, 39% and 32% of patients had received prior biologic therapy, respectively, whereas the proposed Australian clinical management algorithm positions deucravacitinib before treatment with biologics. Differences between the trial populations and the proposed Australian population in terms of prior biologic therapy may limit the applicability of the trial results. The ESC considered these applicability issues result in uncertainty regarding the treatment effect that might be observed in clinical practice. The Pre-PBAC Response noted the PSCR presented additional subgroup analyses (by prior methotrexate and no prior biologic use) which indicated the treatment effect relative to apremilast was maintained in the proposed PBS population (paragraph 6.34 refers).

6.47 The submission described deucravacitinib as non-inferior in terms of safety compared to apremilast based on safety outcomes. The evaluation considered this claim was adequately supported; however, there is a lack of long-term safety data for deucravacitinib.

6.48 The PBAC considered that the claim of superior comparative effectiveness to apremilast was reasonable; however, given the place in therapy was uncertain and likely overlapped with biologics to an uncertain degree, the PBAC considered a claim versus biologics may also merit consideration, and noted no evidence was presented in the submission to assess such a claim.

6.49 The PBAC considered that the claim of non-inferior comparative safety to apremilast was reasonable, however noted there was a lack of long-term safety data for deucravacitinib and the TYK2 class of therapies.

Economic analysis

6.50 The submission presented a cost-utility analysis. This is consistent with the claim of superior comparative clinical effectiveness and non-inferior safety of deucravacitinib versus apremilast in patients with severe CPP.

6.51 Table 9 provides a summary of the key components of the model.

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

Component	Summary	Justification/Comments
Type of analysis	Cost-utility analysis	This is consistent with the submission's clinical claim.
Time horizon	5 years in the model base case versus 24 weeks comparative data in the POETYK 1 and POETYK 2 trials	Considered sufficient to capture the downstream treatment implications; consistent with the PBAC cost-effectiveness review of biologics; sensitivity analyses (2 years, 10 years, lifetime) were conducted. The five-year time horizon in the model was long relative to the 24 weeks of comparative data in the POETYK 1 and POETYK 2 trials.
Outcomes	PASI response, mortality, life years, QALYs	The submission considered the use of PASI response to capture treatment effectiveness was appropriate as it was the outcome most used in economic evaluations in severe CPP and PASI 75 response was a primary outcome in the pivotal POETYK trials. These outcomes are reasonable. PASI 75 response at 16 weeks was also the key outcome in the apremilast resubmission considered at the July 2020 PBAC Meeting (Table 1, apremilast, PSD, July 2020 PBAC Meeting).
Methods used to generate results	Markov cohort	This is appropriate and consistent with most economic evaluations identified in the review.
Health states	16 mutually exclusive health states: • 1L treatment[a] (5 states: PASI <50, 50 to <75, 75 to <90, 90 to <100, 100 responses) • bDMARD (5 states: PASI <50, 50 to <75, 75 to <90, 90 to <100, 100 responses) • BSC (5 states: PASI <50, 50 to <75, 75 to <90, 90 to <100, 100 responses) • Death	To capture key clinical outcomes and management algorithm in Australia. The ESC noted the large number of health states used in the economic model.
Cycle length	8 weeks	To capture key time points from clinical trials and clinical practice where patients with PASI score >15 would be eligible for biologics after a minimum of six weeks of treatment. While eight weeks may be long enough to capture treatment response with at least six weeks' treatment with non-biologics, one of the eligibility criteria to initiate biologics, a single cycle is not long enough to capture treatment response with biologics (minimum 12 weeks after initiation).
Transition probabilities or allocation to health states	First-line treatment effectiveness (deucravacitinib or apremilast): Pooled IPD data from the POETYK trials for Weeks 0-24; assumed constant thereafter, i.e., patients remained in the same PASI response health state until treatment discontinuation (assumed 0% in the base case) or death.	The transition probabilities from the POETYK trials to the modelled PBS population may be confounded by only 25.5% of the trial participants had prior methotrexate, while 34.8% received prior biologic systemic treatment. The proposed PBS eligibility required patients to have failed methotrexate treatment and the proposed clinical positioning of deucravacitinib was for patients not previously treated with biologics. The assumption that patients remained in the same PASI response health state until treatment discontinuation (0% in the base case) or death implicitly assumed no loss of efficacy at all over time which may not be reasonable.

Component	Summary	Justification/Comments
	Biologics treatment effectiveness: PASI responses were from a Bayesian network meta-analysis (Armstrong 2022[4]) and applied in the first cycle on biologics treatment; assumed constant thereafter. To simplify the model structure, the submission applied the cumulative effectiveness of three sequential lines of biologics at the first cycle of biologic treatment (risankizumab, bimekizumab and guselkumab).	The application of cumulative effectiveness of three consecutive biologics at the first cycle of biologic treatment was inconsistent with clinical practice, though favouring apremilast. While bimekizumab received positive PBAC recommendation as the tenth biologic treatment in severe CPP in March 2022 (paragraph 7.1, bimekizumab, PSD, March 2022 PBAC Meeting), it was not PBS-listed at the time of evaluation.
	Subsequent treatment: assumed all patients with PASI score >15 would receive biologics treatment (proportion of patients with PASI score >15 at 8, 16, 24 weeks were from IPD from the POETYK trials); assumed no patients transition to biologics beyond 24 weeks.	While the threshold for switching was consistent with the PBS criterion for initiation of biologic treatment, the timing of switch may be reasonable. The PBS requires that assessment of response must be conducted after a minimum of 12 weeks of therapy. Nevertheless, earlier application of treatment effect from biologics favours apremilast.
	BSC: PASI response rates from the placebo groups of the POETYK trials were used to distribute patients between PASI response health state 8 weeks post initiation of BSC. After 8 weeks, constant transition probabilities were assumed.	To capture patients who discontinue treatment after exhausting available systemic treatment (non-biologic, biologic). The model only allowed for one-directional flow of treatments (i.e., from deucravacitinib/apremilast to biologic) but not switching among non-biologic systemics (e.g., from deucravacitinib to apremilast/ciclosporin/acitretin), nor allowed for patients (e.g., those who achieved adequate treatment response) to switch from biologics back to non-biologic oral therapy, a possibility in clinical practice.
	Mortality: baseline risk from ABS (Life Tables, 2018-2020)[5]; increased mortality risk from psoriasis from literature; no difference in mortality between deucravacitinib and apremilast treatment.	No difference in mortality between deucravacitinib and apremilast in the POETYK trials. Some literature[6] considered that there is no evidence that psoriasis increases the risk of death. Death not included in model in the CER biologics review.
Health-related quality of life	Literature-based (Zug 1995[7]): 0.59 for PASI <50, 50 to <75 responses. 0.89 for PASI 75 to <90, 90 to <100, 100 responses.	Based on stated prior PBAC acceptance and considerations including the CER on biologics for the treatment of severe CPP considered at the July 2020 PBAC Meeting.

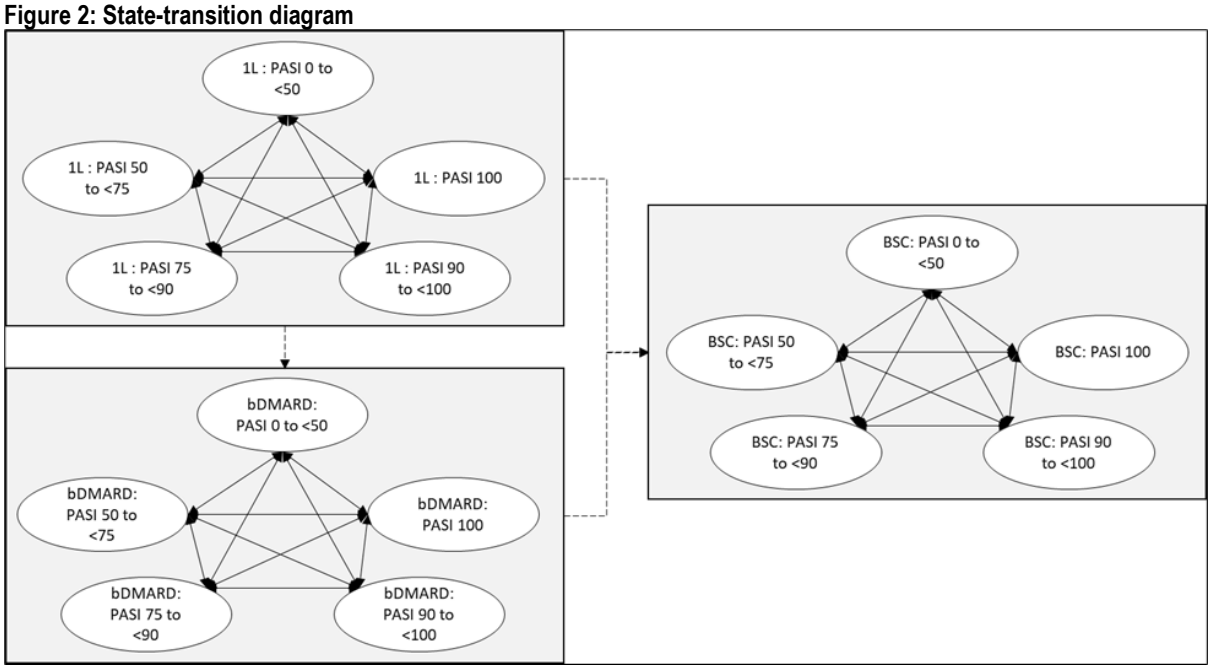
Source: Tables 49 and 87, pp111 and 155 of the submission.
1L = first line (deucravacitinib / apremilast); ABS = Australian Bureau of Statistics; BSC = best supportive care; CER = cost-effectiveness review; CPP = chronic plaque psoriasis; IPD = individual patient data; PASI = Psoriasis Area and Severity Index; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; QALYs = quality-adjusted life years.
PASI 75 response assessed as a proportion of subjects who achieved at least a 75% improvement from baseline in the PASI score.

[4] Armstrong AW, Soliman AM, Betts KA, et al. Long-Term Benefit–Risk Profiles of Treatments for Moderate-to-Severe Plaque Psoriasis: A Network Meta-Analysis. *Dermatology and therapy*. 2022 Jan;12(1):167-84.
[5] *Life tables, 2018-2020*, Australian Bureau of Statistics, released 4 November 2021.
[6] Hendrix N, Ollendorf DA, Chapman RH, Loos A, Liu S, Kumar V, Linder JA, Pearson SD, Veenstra DL. Cost-Effectiveness of Targeted Pharmacotherapy for Moderate to Severe Plaque Psoriasis. *J Manag Care Spec Pharm*. 2018 Dec;24(12):1210-1217.
[7] Zug KA, Littenberg B, Baughman RD, et al. Assessing the preferences of patients with psoriasis: a quantitative, utility approach. *Archives of Dermatology*. 1995 May 1;131(5):561-8.

[a] The submission reported that while technically, deucravacitinib/apremilast treatment could be considered in a second-line setting owing to its requirement for prior methotrexate use, it was considered the first-line treatment within the context of the model (p111 of the submission).

6.52 The submission incorporated four patient-relevant outcomes in the model structure: treatment effectiveness (PASI response), PASI response to subsequent treatment (biologics), treatment discontinuation (best supportive care, BSC) and mortality. A Markov cohort approach was used to distribute patients between 16 mutually exclusive health states where patients transition between PASI response health states (PASI <50, PASI 50 to <75, PASI 75 to <90, PASI 90 to <100 and PASI 100 responses) within each line of therapy (first line (1L), deucravacitinib or apremilast; bDMARDs). Figure 2 presents the state-transition diagram.

Figure 2: State-transition diagram



Source: Figure 27, p125 of the submission.
1L = first line (deucravacitinib / apremilast); bDMARD = biologic disease-modifying antirheumatic drug; BSC = best supportive care; PASI = Psoriasis Area and Severity Index.

6.53 All patients initiating treatment, deucravacitinib or apremilast, referred to as first-line or 1L treatment in the economic model, were assigned a risk of mortality (based on age and sex). Those who survived either remained on treatment or discontinued treatment (set as 0% in the base case). Patients who failed to achieve an adequate response with first-line treatment and had a PASI score of >15 switched to biologics therapy. All BSC patients were assumed to have PASI <50 response in the first treatment cycle. Individual patient data (IPD) from the POETYK 1 and POETYK 2 trials were used to distribute patients to the various first-line PASI response health states for the first three 8-week model cycles (24 weeks). Afterwards, treatment effectiveness was assumed constant. For biologic PASI response health states, the submission assumed biologics treatment as a single course of therapy with effectiveness based on the cumulative effectiveness of three lines of biologics and

attributed within the first cycle on treatment. Constant effectiveness was applied after the first cycle. Treatment discontinuation was incorporated in the model to allow patients to transition from first line treatment (deucravacitinib/apremilast) health states to BSC health states (for sensitivity analyses).

6.54 The base case incremental cost-effectiveness ratio (ICER), based on the effective price of deucravacitinib and the published price of apremilast, was estimated to be $25,000 to < $35,000/QALY gained. The key model drivers are given in the table below.

Table 10: Key drivers of the model

Description	Method/Value	Impact Base case: $[redacted][1]/ additional QALY gained
Utilities	Utility values for PASI response health states from literature (Zug 1995)	High, base case favours deucravacitinib. Use of pooled POETYK trial data increased the ICER by 510% to $[redacted][2] / additional QALY gained.
Subsequent biologics use	Biologic use based on the POETYK trials[a]	Moderate, base case favours deucravacitinib. Use of other assumption (e.g., all patients with PASI <50 response transition to biologics) increased the ICER by 74% to $[redacted][3] / QALY gained.
Clinical effectiveness of deucravacitinib / apremilast	Distribution of PASI response health states based on pooled IPD data of the POETYK 1 and POETYK 2 trials	High. Use of data from POETYK 2 alone increased the ICER by 92% to $[redacted][4] / QALY and use of data from POETYK 1 decreased the ICER by 47% to $[redacted][5] / QALY.
Loss of efficacy (post 24 weeks)	Assumed no loss of efficacy post 24 weeks for both deucravacitinib and apremilast	High, base case favours deucravacitinib. Assuming 10% loss of efficacy for deucravacitinib and apremilast increased the ICER by 25% to $[redacted][6] / QALY.

Source: Tables 105-107, pp170-171 of the submission

ICER = incremental cost-effectiveness ratio; IPD = individual patient data; PASI = Psoriasis Area and Severity Index; QALY = quality-adjusted life year.

[a] IPD from the POETYK trials were used to derive the proportion of patients in each PASI response health state with an absolute PASI score >15 at week 8, 16 and 24. All of these patients were switched to biologics, assuming all patients would transition to biologics once eligible. Sensitivity analyses explored the impact of varying proportions of patients not achieving PASI >75 response switching to biologics.

The redacted values correspond to the following ranges:

[1] *$25,000 to < $35,000*

[2] *$155,000 to < $255,000*

[3] *$45,000 to < $55,000*

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

[5] *$15,000 to < $25,000*

[6] *$35,000 to < $45,000*

6.55 The economic model was most sensitive to utility values, first-line (deucravacitinib or apremilast) clinical effectiveness, efficacy post 24 weeks trial period, and subsequent biologic use.

6.56 Table 11 presents the results of the stepped economic evaluation in the submission. These results were based on the proposed effective price of deucravacitinib and the published prices of apremilast and adalimumab.

Table 11: Results of the stepped economic evaluation

Step and component	Deucravacitinib	Apremilast	Increment	Incremental cost / extra outcome gained
Step 1: Trial-based (24 weeks): Pooled POETKY trials				
Costs (1L drug costs)	$	$3,683	$	
PASI 50 response	78.5%	55.5%	23.0%	$
PASI 75 response	63.0%	37.9%	25.1%	$
PASI 90 response	36.5%	20.6%	15.8%	$
PASI 100 response	14.9%	6.6%	8.2%	$
Step 2: Translation of PASI response outcomes to QALYs				
Costs	$	$3,683	$	
QALYs	NR	NR	0.0192	
Incremental cost/extra QALY gained				$ [1]
Step 3: Extrapolation of costs and outcomes (to 5-year time horizon)				
Costs	$	$36,693	$	
QALYs	3.5147	3.1869	0.3277	
Incremental cost/extra QALY gained				$ [2]
Step 4: Incorporation of subsequent therapy with biologics				
Costs	$	$42,853	$	
QALYs	3.7370	3.6228	0.1142	
Incremental cost/extra QALY gained (base case)				**$** [3]

Source: Tables 98-99 and 102, pp162 and 166-168 of the submission; Attachment 13 – Deucravacitinib CPP economic evaluation of the submission.

1L = first line (deucravacitinib / apremilast); PASI = Psoriasis Area and Severity Index; QALY = quality adjusted life year.

The redacted values correspond to the following ranges:

[1] *$35,000 to < $45,000*

[2] *$15,000 to < $25,000*

[3] *$25,000 to < $35,000*

6.57 The results of key univariate and a multivariate sensitivity analysis, based on the effective price of deucravacitinib and the published prices of apremilast and adalimumab, are summarised in Table 12.

Table 12: Results of selected univariate sensitivity analyses presented in the submission

Analyses	Incremental cost ($)	Incremental QALY	ICER ($)	% change to ICER
Base case	[redacted]	**0.1142**	[redacted][1]	
Discount rate				
Discount rate (base case 5% costs and outcomes)				
• 0% costs and outcomes	[redacted]	0.1261	[redacted][1]	-0.1%
• 3.5% costs and outcomes		0.1175	[redacted][1]	0.0%
Clinical effectiveness				
Trial-period (0-24 weeks) (base case: pooled POETYK data)				
• POETYK 1	[redacted]	0.1913	[redacted][2]	-46.6%
• POETYK 2		0.0634	[redacted][3]	91.9%
Loss of efficacy per year[a] (post 24 weeks) (base case: 0%)				
• Deucravacitinib: 10%; apremilast: 10% **(A)**	[redacted]	0.0911	[redacted][4]	25.4%
• Deucravacitinib: 20%; apremilast: 10%		0.0664	[redacted][5]	72.0%
Biologic use				
Proportion of patients receiving biologics[b] (base case: trial-based[c])				
• PASI <50: 100%; PASI 50 to <75: 100%	[redacted]	0.0250	[redacted][5]	64.5%
• PASI <50: 100%; PASI 50 to <75: 50%		0.0377	[redacted][5]	71.0%
• PASI <50: 100%		0.0503	[redacted][5]	74.2%
• PASI <50: 50%		0.1890	[redacted][1]	-9.4%
• 0% (Step 3 of economic evaluation, Table 11)		0.3277	[redacted][2]	-22.3%
Utility values				
Utility data source (base case: Zug 1995; severe psoriasis)				
• Pooled POETYK trial data (Model 1[d]) **(B)**	[redacted]	0.0187	[redacted][6]	509.8%
• Pooled POETYK trial data (Model 3[d])		0.0145	[redacted][6]	687.9%
• Zug 1995[8] (moderate psoriasis)		0.0381	[redacted][7]	200.0%
• Sherif 2017 (UK tariffs)		0.0290	[redacted][8]	294.2%
• Bewley 2018[9]		0.0524	[redacted][3]	117.9%
Multivariate analysis				
A + B	[redacted]	0.0160	[redacted][6]	615.2%
A + B with an 8.5% reduction in deucravacitinib DPMQ		0.0160	[redacted][1]	0.0%

Source: Tables 104-109, pp169-172 of the submission.

BSC = best supportive care; ICER = incremental cost-effectiveness ratio; PASI = Psoriasis Area and Severity Index; QALY = quality adjusted life year.

[a] Proportion of patients transitioning to the next most severe health state in the following cycle.

[b] The proportion of patients in each PASI response health state that are transitioned to biologics each cycle, post 24 weeks.

[c] Biologic use in the base case was estimated based on the proportion of patients with a PASI score >15 at week 8, 16 and 24 in the POETYK trials.

[d] The submission used three linear regression models to estimate EQ-5D utility values (Australian weights) based on PASI response at Week 16 in the POETYK trials. Model 1 adjusted for baseline EQ-5D utility score. Model 3 adjusted for baseline EQ-5D, treatment arm, prior biologic exposure (yes/no), prior systemic therapy (yes/no), and body weight (≥90 kg and <90 kg) at baseline.

The redacted values correspond to the following ranges:

[1] $25,000 to < $35,000
[2] $15,000 to < $25,000
[3] $55,000 to < $75,000
[4] $35,000 to < $45,000
[5] $45,000 to < $55,000
[6] $155,000 to < $255,000

[8] Zug KA, Littenberg B, Baughman RD, Kneeland T, Nease RF, Sumner W, O'Connor GT, Jones R, Morrison E, Cimis R. Assessing the preferences of patients with psoriasis: a quantitative, utility approach. *Archives of Dermatology*. 1995 May 1;131(5):561-8.

[9] Bewley A, Barker J, Mughal F, Cawston H, Damera V, Morris J, Tencer T. Cost-effectiveness of apremilast in moderate to severe psoriasis in the United Kingdom. *Cogent Medicine*. 2018 Jan 1;5(1):1495593.

[7] *$75,000 to < $95,000* [8] *$115,000 to < $135,000*

6.59 The ESC considered the relevance of the PASI response rates from the POETYK trials to the modelled PBS population were likely to be confounded to some extent:

- Only 25.5% of the trial participants had methotrexate as prior and ongoing psoriasis-related medication,[10] whereas the proposed PBS restriction is for patients who have not responded to, or are intolerant of, methotrexate.
- 34.8% of the trial participants had prior biologic systemic treatment,[11] whereas the proposed PBS restriction is for patients who have not previously received biologics.

6.60 The Pre-PBAC Response stated the subgroup analyses presented in the PSCR indicated prior treatment use was not a significant treatment effect modifier and therefore argued the PASI response rates from the POETYK trials were applicable to the PBS population.

6.61 The assumption that patients remained in the same PASI response health state until treatment discontinuation (0% in the base case) or death implicitly assumed no loss of efficacy over time which may not be reasonable. Sensitivity analyses showed that the ICER was moderately sensitive to the assumed loss of efficacy of deucravacitinib and apremilast after the trial follow up period. The ESC considered the base case assumption of no decline in treatment effect over time was unrealistic and advised the model should include an assumption of declining treatment effect over time for both deucravacitinib and apremilast at similar rates.

6.62 The submission considered that the model was moderately sensitive to subsequent biologic use. The base case assumption of subsequent biologic use among patients with a PASI >15 after at least six weeks of treatment with deucravacitinib or apremilast aligned with expected clinical practice. This assumption was conservative for the cost-effectiveness of deucravacitinib: when use of subsequent biologics was removed, the ICER decreased from $25,000 to < $35,000 to $15,000 to < $25,000 per QALY gained.

6.63 The cost-effectiveness of deucravacitinib was very sensitive to the choice of utilities. In the base case, the submission used utilities from Zug (1995) (Table 13), citing the PBAC's prior acceptance of this source and considerations in the cost-effectiveness review of biologics for the treatment of chronic plaque psoriasis considered at the July 2020 PBAC Meeting. However, EQ-5D data were collected in the POETYK trials. The PBAC Guidelines (p77) state a preference for trial-based utilities when there no significant concerns about the reliability and relevance of the utilities. The PBAC Guidelines (p77) state "Where utility weights or QALY changes cannot be directly estimated from data collected in the clinical studies from Section 2, or there are significant concerns about the reliability and relevance of trial-based utility", then

[10] Table S.4.3.2, p119 of the POETYK 1 CSR Supplementary Tables; Table S.4.3.2, p147 of the POETYK 2 CSR Supplementary Tables.
[11] POETYK 1 trial: 38.9% (p80 of the POETYK 1 CSR) POETYK 2 trial: 32.1% (p94 of the POETYK 2 CSR).

"additional studies (either published or done for the submission) may be needed to estimate utility weights for health states in the economic model." The evaluation considered that, on balance, the EQ-5D data from the POETYK trials may be a more appropriate source of utilities. When these utilities were used, the ICER (based on the published prices of apremilast and adalimumab) increased substantially, from $25,000 to < $35,000 to $155,000 to < $255,000 per additional QALY gained.

Table 13: Utility value data sources available in the economic model in the submission

	PASI <50	PASI 50 to <75	PASI 75 to <90	PASI 90 to <100	PASI 100
Base case					
Zug 1995 (severe, PASI score >15)	0.590	0.590	0.890	0.890	0.890
Other sources					
Zug 1995 (moderate, PASI score ≥12 to ≤15)	0.790	0.790	0.890	0.890	0.890
Pooled POETYK trial data[a]					
Model 1	0.844	0.882	0.895	0.921	0.923
Model 2	0.848	0.878	0.888	0.914	0.914
Model 3	0.856	0.887	0.896	0.920	0.919

Source: Tab "Inputs" in Attachment 13 of the submission; Table 52, p116 of the submission.
PASI = Psoriasis Area and Severity Index.
[a] The submission used three linear regression models to estimate EQ-5D utility values (Australian weights) based on PASI response at Week 16 in the POETYK trials. Model 1 adjusted for baseline EQ-5D utility score. Model 3 adjusted for baseline EQ-5D, treatment arm, prior biologic exposure (yes/no), prior systemic therapy (yes/no), and body weight (≥90 kg and <90 kg) at baseline (p149 of the submission).

6.64 The PSCR argued the use of the Zug (1995) utilities were appropriate on the basis the PBAC have previously established the importance of Zug (1995) as a precedent in evaluating the cost-effectiveness of psoriasis medicines, stating that "if alternative utilities were used this would alter the ICER for the PASI > 15 population previously accepted by the PBAC" (July 2020 cost-effectiveness review PSD, paragraph 4.10). The PSCR further argued the precedent of using the Zug (1995) utilities is applicable to the current evaluation due to the downstream implications (in terms of both costs and QALY gains) of patients moving to biologics, and the potential for misspecification of the value of superior response rates with deucravacitinib compared to apremilast.

6.65 Overall, the ESC noted while the Zug (1995) utilities would be consistent with previous PBAC considerations and the post-market review of biologics for severe CPP, it did not agree with the PSCR that the Zug (1995) utilities should be considered the most appropriate utilities. The ESC considered there were issues with the Zug (1995) methodology, such as the mapping of the proportion of skin affected to PASI scores (i.e. severity weighted by area) and did not consider consistency alone was an adequate reason to accept one set of utilities over another. In addition, the ESC noted an implausibly large difference between utility scores in the PASI 50-75 (0.59) and PASI 75-90 (0.89) and was uncertain if Zug (1995) were the most appropriate set of utilities for the model, given these apparent issues. The ESC therefore considered the utilities collected in the POETYK trials were likely a more reliable basis upon which to model the cost-effectiveness of deucravacitinib. The ESC noted that the base case model in the submission used Model 1 to adjust utilities had the lowest AIC/BIC scores,

indicating the best statistical fit, and appeared to have face validity (Table 13). The ESC considered the use of Model 1 utilities appeared to be reasonable.

6.66 The Pre-PBAC Response stated that prior PBAC decision-making in the CPP cost effectiveness review had highlighted the overall lack of consistency in published utility values for CPP and argued the PBAC appeared to have 'opted for consistency' over sponsor-specific utility values, and further argued it was appropriate for the same approach to be applied for deucravacitinib. Further, the Response stated that while the ICER change with trial-based utilities seems large compared to the use of the Zug utilities, also noted that change is reversed with a less than 10% change in the price of deucravacitinib (based on published prices), and argued this was because those same utility values which appear to favour apremilast over deucravacitinib also underestimate the PBAC's accepted value of biologics.

6.67 Apart from the drug costs of deucravacitinib and apremilast, the submission assumed that there was no other difference in the costs associated with treatment with deucravacitinib and apremilast. However, the draft Product Information (p2) for deucravacitinib recommends evaluation of tuberculosis infection prior to initiation and the monitoring for the signs and symptoms of active tuberculosis while on treatment.

6.68 The ESC considered the structure of the model was overall likely to be reliable to assess the cost-effectiveness of deucravacitinib and apremilast, however advised its preferred revised base case (for this comparison) should include a 10% per year reduction in efficacy (after 24 weeks) for both deucravacitinib and apremilast and should use utilities derived from the pooled POETYK trial data. The ESC noted the revised base case ICER based on published prices was $155,000 to < $255,000 per QALY (615% higher than the submission base case) (refer Table 12.

6.70 **Table 12**).

6.71 The Pre-PBAC Response accepted the ESC view to apply a waning treatment effect to both deucravacitinib and apremilast, however for reasons outlined in paragraphs 6.64 and 6.66, did not agree with using trial-based utilities in the model.

6.72 Given its view that biologics are also relevant comparators, the ESC considered it may be informative to model the cost-effectiveness of deucravacitinib and biologics to fully assess the cost-effectiveness of deucravacitinib in the broader CPP treatment landscape. The Pre-PBAC Response argued a comparison with biologics would not provide the PBAC with any information on the cost-effectiveness of deucravacitinib in the proposed second line setting and would not support the proposed PBS restriction for deucravacitinib. The Response also argued any comparison against biologics would ultimately rely on an indirect treatment comparison, the results of which may be difficult to interpret if non-inferiority is not established, resulting in the need to undertake a south-west quadrant cost effectiveness analysis.

Drug cost/patient/year

6.73 The deucravacitinib and apremilast drug costs per patient per year used in the submission are presented in Table 14.

Table 14: Drug cost per patient for deucravacitinib and apremilast (using effective price for deucravacitinib, published price for apremilast)

	Economic model and financial estimates	
	Deucravacitinib	**Apremilast**
Mean dose, mg	6 mg once daily	30 mg twice daily (after titration)
Duration, days		
Year 1 Year 2	365.25 365.25	Titration: 14; maintenance: 350.25[a] Maintenance: 365.25
Compliance, %	[redacted] [A]	94.7[o] [B]
DPMQ	Effective DPMQ: $[redacted] [C]	Published DPMQ: $272.29 (titration pack) [D], $652.80 (maintenance pack) [E]
Scripts/Year 1	[redacted][1] [F=365.25/28 x A]	Titration pack: 1 [G] Maintenance pack: 11.85 [H=350.25/28 x B]
Scripts/Year 2	Same as Year 1	Maintenance pack: 12.35[I=365.25/28 x B]
Cost/patient		
Year 1	$[redacted] [J=C x F]	Titration: $272.29 [L = D x G] Maintenance: $7,733.04 [M = E x H]
Year 2	$[redacted] [K=C x F]	Maintenance: $8,064.22 [N = E x I]
First 2 years	$[redacted] [= J + K]	$16,069.55 [= L + M + N]

Source: table constructed during the evaluation based on information provided in the economic and financial models supplied with the submission. Tables 89-91, pp157-158 and 176 of the submission.

DPMQ = Dispensed Price for Maximum Quantity.

[a] 350.25 = 365.25-15 in the submission. It is not clear why the submission minus 15 rather than 14 to account for the apremilast starting titration pack).

The redacted value correspond to the following range:

[1] < 500

Estimated PBS usage & financial implications

6.74 This submission was considered by DUSC. The submission used an epidemiological approach to estimate the number of eligible patients.

6.75 Table 15 outlines the key inputs relied on in the financial estimates.

Table 15: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Prevalent population	Prevalence of 2.64% based on the estimate used in the minor apremilast resubmission considered by the PBAC at the July 2020 PBAC Meeting.	The DUSC previously considered the prevalence estimate of 3.3% should be reduced 10-20% to account for plaque psoriasis (Table 10, paragraph 5.11, apremilast PSD, July 2020 PBAC Meeting).
Uptake rate	10% in Year 1 increasing to 40% in Year 6. Based on Advisory Board.	The impact of +5% or -5% on uptake rates were tested in sensitivity analysis. Based on clinical opinion, estimates uncertain. Higher uptake rates would result in greater number of patients treated with deucravacitinib.
Dose/duration	Dose regimen was as per drafted PI, 12 months	Consistent with the dose/duration in the economic evaluation
Offsets	Offsets for apremilast (51%), ciclosporin (11%), acitretin (13% and phototherapy (25%)	Proportional split of substitution among other non-biologic systemics was estimated based on clinical opinion. Offsets for ciclosporin, acitretin and phototherapy not included in economic evaluation. Furthermore, economic evaluation included the cost of subsequent biologics, whereas financial estimates did not.
Phototherapy	80% benefit of MBS item 14050 (100% fee: $54.90). Assumed 54 services/patient/year (Sullivan 2009).[12]	MBS 14050 (100% fee should be $55.80). Low impact on the overall health budget.
Pre-screening and monitoring for ciclosporin	80% benefit of MBS item 66500 (100% fee $9.70);14.5 services/patient/year	The submission omitted the costs associated with the pre-treatment evaluation of tuberculosis and the monitoring for the signs and symptoms of active tuberculosis in patients receiving deucravacitinib. This is not appropriate and favours deucravacitinib. Also, several MBS items were included for monitoring costs for apremilast and ciclosporin in the apremilast submission (Table 6, paragraph 5.5, apremilast PSD, July 2020 PBAC Meeting). Nevertheless, likely low impact on the overall health budget.
Pre-screening and monitoring for acitretin	80% benefit of MBS item 66512 (100% fee $17.70); 4 services/patient/year	

Source: Table 114, p175 of the submission; MBS online. Italicised text added during the evaluation.
DUSC = Drug Utilisation Sub Committee; MBS = Medicare Benefits Schedule; PBAC = Pharmaceutical Benefits Advisory Committee; PI = product information; PSD = public summary document.
[a] The submission reported that based on (Sullivan & Preda, 2009), a standard treatment course for phototherapy in Australia was 3 times a week for a period of 6-12 weeks, which usually provided patients with 3-6 months of improved disease control.

[12] Sullivan, J. R., & Preda, V. A. (2009). Treatments for severe psoriasis. *Australian Prescriber*, 32(1), 14-18. The submission reported that a standard treatment course of phototherapy was 3 times a week, for 6-12 weeks, providing patients with 3-6 months of improved disease control. Taking a median of 9 weeks' treatment per course and two courses per year, the submission assumed 54 services per patient per year.

6.76 Table 16 presents the estimated use and financial implications of the proposed listing, based on the proposed effective price for deucravacitinib and published prices for other treatments.

Table 16: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients eligible	[1]	[1]	[1]	[1]	[1]	[1]
Uptake	10%	20%	25%	30%	35%	40%
Number of patients treated	[2]	[7]	[7]	[7]	[7]	[16]
Number of scripts dispensed[a]	[3]	[8]	[10]	[13]	[13]	[13]
Estimated financial implications of deucravacitinib (effective price)						
Cost to PBS/RPBS less co-payments[b]	[4]	[9]	[11]	[14]	[15]	[17]
Estimated financial implications for substitution of other medicines (published prices)						
Cost to PBS/RPBS less co-payments[b] ($)	[5]	[5]	[5]	[5]	[5]	[5]
Net financial implications						
Net cost to PBS/RPBS[b] ($)	[6]	[4]	[12]	[12]	[9]	[18]
Net cost to MBS ($)	[5]	[5]	[5]	[5]	[5]	[5]
Net cost to PBS/RPBS/MBS[b] ($)	[6]	[4]	[4]	[12]	[9]	[9]

Source: Tables 111, 115, 118, 120, 122, 125 and 127, pp176-177, 179, 181-182 and 184-185 of the submission.
MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Schedule of Pharmaceutical Benefits.
[a] Assuming 12.43 scripts per year as estimated by the submission [12.43 = (365.25/28) x 95.3% where compliance = 95.3% based on POETYK 1 and POETYK 2 trials].
[b] Note that the estimated costs to the PBS/RPBS used the AHI and dispensing fees and patient co-payments before July 2022.
The redacted values correspond to the following ranges:

[1] 20,000 to < 30,000	*[10] 80,000 to < 90,000*
[2] 500 to < 5,000	*[11] $60 million to < $70 million*
[3] 30,000 to < 40,000	*[12] $30 million to < $40 million*
[4] $20 million to < $30 million	*[13] 100,000 to < 200,000*
[5] net cost saving	*[14] $70 million to < $80 million*
[6] $10 million to < $20 million	*[15] $90 million to < $100 million*
[7] 5,000 to < 10,000	*[16] 10,000 to < 20,000*
[8] 60,000 to < 70,000	*[17] $100 million to < $200 million*
[9] $40 million to < $50 million	*[18] $50 million to < $60 million*

6.77 The total net cost to the PBS/RPBS of listing deucravacitinib was estimated to be $40 million to < $50 million in Year 6, and a total of $100 million to < $200 million in the first 6 years of listing.

6.78 The submission indicated that should the PBAC recommend deucravacitinib, further adjustment would be required to the overall net cost to the health budget as the current proposed effective price for deucravacitinib was based on the published prices for apremilast prices.

6.79 The submission reported that the financial estimates were most sensitive to prevalence, the proportion of patients treated by a dermatologist or experienced general physician and uptake rates. If cost-offsets from anticipated decreased use of biologics with the proposed listing were included and based on the modelled time on treatment over five years, the submission estimated the net cost to the health budget (using the published price of adalimumab as a proxy for all biologics):

$30 million to < $40 million in Year 6, and a total of $100 million to < $200 million in the first six years of listing (a reduction in the net cost of 28.4%).

6.80 The DUSC considered that overall, the estimates presented in the submission are overestimated. The DUSC considered the main issues to be:

- The place in therapy for deucravacitinib is complex. The submission proposed that the comparator for deucravacitinib is apremilast and positioned apremilast between non-biologic systemic therapies and biologic disease-modifying antirheumatic drugs (bDMARDs). The submission assumed that the market for apremilast is separate to bDMARDs however the proposed restriction would permit switching between apremilast and bDMARDs. DUSC considered that a revised financial estimates model based on a mixed epidemiological and market share approach would be appropriate to account for substitution of both non-biologic systemic agents and bDMARDs with deucravacitinib.
- The estimate of substituted apremilast scripts is likely an overestimate, as it is substantially more (n=10,000 to < 20,000) than the actual number of scripts for apremilast in its first year of listing (January to December 2021, n=13,849).
- The treatment uptake is potentially overestimated as prescribing is limited to dermatologists and will also depend on the familiarity of prescribers with deucravacitinib.

6.81 The Pre-PBAC Response noted the DUSC advice and stated:

- While there were 12,606 apremilast scripts dispensed in the first year of listing, the second year (at time of response) had reached 14,585 and stated that the estimated full second year of listing on a pro rata basis, was 21,878 apremilast scripts, an increase of 73.5% compared to the first year. The Response therefore argued the number of apremilast scripts will continue to grow in the absence of PBS listing for deucravacitinib;
- Furthermore, given the differing efficacy and safety profiles of apremilast and biologics, it was reasonable to expect low or no switching from biologics to apremilast; and
- The treatment uptake is likely to change with the change to treatment criteria implemented in September 2022 that allow accredited dermatology registrars to prescribe apremilast (and by extension deucravacitinib).

Quality Use of Medicines

6.82 The submission stated its commitment to support the safe and effective use of deucravacitinib in Australia and its adherence to the Code of Conduct of Medicines Australia:

- Physician education: Field medical representatives currently provide education for dermatologists (and related specialties) on the clinical management of patients with psoriasis, the therapeutic landscape, and the mechanism of the TYK2 pathway

and its role in psoriasis pathogenesis. After TGA registration and PBS approved listing, physician education will focus on deucravacitinib mechanism of action, clinical data relevant to the Australian patient management, patient eligibility for treatment, adverse event symptom identification, and adverse event management as appropriate and required.

- Risk Management Plan (RMP): The submission reported that the RMP for deucravacitinib in Australia contains a description and analysis of the safety profile of deucravacitinib including a summary of the safety concerns. Two types of safety concerns are outlined: Important Potential Risks (serious infections and malignancies, EU-RMP) and Missing Information (use in pregnancy, lactation and long-term safety, EU-RMP). The pharmacovigilance plan for deucravacitinib includes routine pharmacovigilance (adverse event reporting, aggregate reports, routine and targeted follow-up, signal detection).
- Educational Materials & Tools: After the listing of deucravacitinib on the PBS, educational resources specific to deucravacitinib and the role of the TYK2 pathway in psoriasis, will be available for both health care professionals and patients. Materials would not be provided directly to the patient but rather through dermatologists and their speciality nurse support staff.

6.83 The DUSC noted that the mechanism of action of deucravacitinib is similar to that of Janus kinase (JAK) inhibitors, and these carry an FDA black box warning and are currently included in the TGA Black Triangle Scheme. However, deucravacitinib does not carry the same warnings, possibly partially due to its short duration of experience. DUSC noted that there is no such signal seen as yet for TYK2 inhibitors. DUSC noted the submission did not include any proposed post-marketing surveillance studies however included a risk management plan for potential risks and an educational program.

Financial Management – Risk Sharing Arrangements

6.84 The submission did not propose any risk sharing arrangement (RSA). The PBAC previously considered a RSA would be reasonable for apremilast to manage the significant uncertainty associated with utilisation estimates (paragraph 6.8, apremilast, PSD, July 2020 PBAC meeting).

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

7 PBAC Outcome

7.1 The PBAC deferred making a recommendation for the listing of deucravacitinib for the treatment of severe chronic plaque psoriasis, to seek additional expert clinical advice on its appropriate and likely place in therapy. In deferring the matter, the PBAC was uncertain as to whether the proposed clinical place of deucravacitinib, in the same line of therapy as apremilast, i.e. after non- or inadequate

response/intolerance/contraindication to methotrexate, but prior to treatment with biologics was reflective of its appropriate use in practice, and whether there was potentially a substantial overlap with the population eligible for biologics. The PBAC requested further dermatology expert clinical advice to resolve this uncertainty, as the cost-effectiveness proposition of deucravacitinib was dependent on the likely place in therapy and most appropriate comparator selection.

7.2 The PBAC noted the submission nominated apremilast as the primary comparator and considered that if the proposed place in therapy were accepted, apremilast was an appropriate comparator. However, the Committee considered that if deucravacitinib was more likely to be used in patients who are potentially eligible for biologics, these therapies may represent a more appropriate primary comparator.

7.3 The PBAC considered the requested listing, which was the same as the apremilast listing, was reasonable if the clinical place proposed in the submission were accepted. However, the PBAC considered it would be reasonable to add a clause to the listings of both deucravacitinib and apremilast excluding concomitant therapy, if listed on that basis. The PBAC also noted the possibility of flow ons to other medicines for CPP pending the place of therapy.

7.4 The PBAC noted the submission was supported by a meta-analysed data set from two, high quality, 3-arm randomised clinical trials comparing deucravacitinib, apremilast and placebo (POETYK 1 and 2), however noted the primary comparisons were for each of the active therapies versus placebo, and the comparison of deucravacitinib and apremilast were based on secondary comparisons. Furthermore, the PBAC noted a reasonable proportion of the populations recruited into the studies had received prior biologics (39% and 32% for POETYK 1 and 2, respectively). The Committee considered the extent of prior biologic use was likely not reflective of the submission's proposed place in Australian practice. The PBAC considered this raised questions about the applicability of the evidence and whether there was a substantial overlap of the biologic population and likely deucravacitinib population, which in turn makes the appropriate comparator unclear.

7.5 The PBAC noted the results of the meta-analysed, whole trial comparison of deucravacitinib and apremilast found statistically significant results in favour of deucravacitinib for the outcomes of sPGA 0/1, PASI 75 and DLQI at weeks 16 or 24, and also noted the results of the subgroup analyses by baseline PASI score (>15 versus ≤15) and prior non-biologic therapy were broadly consistent with the whole trial analyses. The PBAC considered the comparative effectiveness in the proposed PBS population (i.e., predominantly biologic naïve) was uncertain given the level of prior biologic use in the POETYK trials, however noted there were relevant subgroup results presented in Warren 2021 (paragraphs 6.36 and 6.38 refer) and the PSCR, which whilst not evaluated, were informative. Considering the totality of the available evidence, the PBAC was satisfied that deucravacitinib is likely to be of superior comparative effectiveness to apremilast, including in the submission proposed PBS population (of

predominantly biologic naïve patients), however there remained residual uncertainty as to the incremental benefit in the PBS population.

7.6 The PBAC noted the submission described deucravacitinib as being of non-inferior comparative safety to apremilast, and considered that based on the available data, this claim was reasonable. However, the PBAC noted there was limited long-term safety data for deucravacitinib, as the first in the TYK2 class of therapies. Furthermore, the Committee noted as the TYK2 pathway was a member of the Janus kinase (JAK) inhibitor family of drugs (albeit different to other existing JAK inhibitors which exert their effects on JAK 1-3 subunits), and it remained uncertain as to whether emerging safety issues with the JAK inhibitor class would also emerge in deucravacitinib in the future.

7.7 The PBAC noted and agreed with the ESC that the structure of the economic model was reasonable for assessing the cost effectiveness of deucravacitinib and apremilast, however also agreed with the ESC that its revised base case, which applied a waning treatment effect to both deucravacitinib and apremilast, and using trial-based utilities, was a more reasonable base case (paragraph 6.68 refers). The PBAC noted the arguments in the PSCR and Pre-PBAC Response regarding the appropriateness of using the Zug (1995) utilities for consistency with prior PBAC considerations (paragraphs 6.64 and 6.66 refer). However, the PBAC agreed with the ESC that there were methodological issues with the Zug (1995) study and an implausibly large difference between utility scores in the PASI 50-75 (0.59) and PASI 75-90 (0.89) (paragraph 6.65 refers). The PBAC considered the utilities collected in the POETYK trials were likely to be a more reliable basis to consider the cost-effectiveness of deucravacitinib. The PBAC noted the revised base case ICER was $155,000 to < $255,000 per QALY using the published prices of apremilast and adalimumab and the ICER using effective prices would be higher.

7.8 When considering the likely utilisation of deucravacitinib in practice, the PBAC agreed with the DUSC and considered the likely use was complex and considered revised estimates, using a mixed market share and epidemiological approach was likely a more reasonable approach. The Committee considered revised estimates of utilisation should be informed by the place in therapy and use in practice.

7.9 The PBAC noted the submission did not provide a basis to consider the comparative effectiveness and safety or cost effectiveness of deucravacitinib to biologics and considered that if this is the appropriate place in therapy, a new submission would likely be required.

Outcome:
Deferred

8 Context for Decision

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

9 Sponsor's Comment

Bristol-Myers Squibb looks forward to working with the PBAC to achieve PBS listing for deucravacitinib in the most timely possible manner.

Addendum to the November 2022 PBAC PSD:

4.02 DEUCRAVACITINIB, Tablet 6 mg, Sotyktu®, Bristol-Myers Squibb Australia Pty Ltd.

10 Background

10.1 In November 2022, the PBAC deferred making a recommendation for the listing of deucravacitinib for the treatment of severe chronic plaque psoriasis, to seek additional expert clinical advice on its appropriate and likely place in therapy (see paragraph **Error! Reference source not found.**).

10.2 Subsequently, the sponsor provided a proposal for consideration. Revisions include:

- A [redacted]% reduction in the price of deucravacitinib (from an ex-manufacturer price (EMP) of $[redacted] to $[redacted]).
- Reduced uptake of deucravacitinib (to address the concern that uptake was likely overestimated, see paragraph **Error! Reference source not found.**).
- Inclusion of offsets for adalimumab (as a proxy for bDMARDs).
- Minor changes to reflect updated mark ups and other minor costs.

10.3 The proposal stated the offer was contingent on the PBAC recommending a PBS restriction for deucravacitinib in line with that previously proposed by the sponsor (i.e., consistent with the restriction criteria for apremilast, see paragraph **Error! Reference source not found.**).

10.4 During its November 2022 consideration, "the PBAC noted and agreed with the ESC that the structure of the economic model was reasonable for assessing the cost effectiveness of deucravacitinib and apremilast, however also agreed with the ESC that its revised base case, which applied a waning treatment effect to both deucravacitinib and apremilast, and using trial-based utilities, was a more reasonable base case*".* Using the revised base case economic model and using the effective EMP proposed for deucravacitinib in November 2022 ($[redacted]), the ICER was $155,000 to < $255,000 per QALY using the published prices of apremilast and adalimumab. The ICER using the confidential prices of apremilast and adalimumab is presented as Scenario A in Table 17**Error! Reference source not found.**.

11 Consideration of the evidence

Economic analysis

11.1 The ICER using the respecified economic model (as described in paragraph 10.4), the revised price of deucravacitinib (EMP $[redacted]) and the confidential prices for apremilast and adalimumab is presented as Scenario B in Table 17**Error! Reference source not found.**.

11.2 The sponsor stated that the proposed price reduction, along with adoption of the Zug utilities (as discussed above in paragraphs 6.63 to 6.66), reduced the ICER to an acceptable range.

Committee in confidence

Table 17: Summary of ICERs

Scenario		ICER
A.	Considered in November 2022, respecified economic model, using effective price of apremilast and indication specific price of adalimumab (as a proxy for bDMARDs)	[redacted]
B.	(A) and using revised price, February 2023	[redacted]

bDMARDs = biologic disease modifying anti-rheumatic drugs; ICER = incremental cost effectiveness ratio; QALY = quality adjusted life year

End committee in confidence

Estimated PBS usage & financial implications

11.3 Table 18 presents the estimated use and financial implications of the proposed listing, based on the revised effective price for deucravacitinib, reduced uptake and published prices for other treatments. The estimates include offsets for reduced use of apremilast, ciclosporin, acitretin and adalimumab (as a proxy for bDMARDs).

Table 18: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients eligible	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Uptake	7.50%	15.00%	22.50%	27.50%	32.50%	32.50%
Number of patients treated	[redacted][2]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Number of scripts dispensed	[redacted][1]	[redacted][4]	[redacted][5]	[redacted][7]	[redacted][8]	[redacted][8]
Estimated scripts of substituted and displaced medicines						
Apremilast	-[redacted][9]	-[redacted][1]	-[redacted][4]	-[redacted][4]	-[redacted][10]	-[redacted][10]
Ciclosporin	-[redacted][2]	-[redacted][2]	-[redacted][2]	-[redacted][3]	-[redacted][3]	-[redacted][3]
Acitretin	-[redacted][2]	-[redacted][2]	-[redacted][2]	-[redacted][3]	-[redacted][3]	-[redacted][3]
Biologics	-[redacted][3]	-[redacted][9]	-[redacted][9]	-[redacted][9]	-[redacted][1]	-[redacted][1]
Estimated financial implications of deucravacitinib (effective price)						
Cost to PBS/RPBS less co-payments ($)	[redacted][11]	[redacted][12]	[redacted][13]	[redacted][13]	[redacted][14]	[redacted][14]
Estimated financial implications for substitution of other medicines (published prices)						
Cost to PBS/RPBS less co-payments($)	[redacted][15]	[redacted][15]	[redacted][15]	[redacted][15]	[redacted][15]	[redacted][15]
Net financial implications						
Net cost to PBS/RPBS($)	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][16]
Net cost to MBS($)	[redacted][15]	[redacted][15]	[redacted][15]	[redacted][15]	[redacted][15]	[redacted][15]
Net cost to PBS/RPBS/MBS($)	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][16]

The redacted values correspond to the following ranges:
[1] 20,000 to < 30,000
[2] 500 to < 5,000
[3] 5,000 to < 10,000
[4]30,000 to < 40,000
[5] 60,000 to < 70,000
[6] 80,000 to < 90,000
[7] 90,000 to < 100,000
[8] 100,000 to < 200,000
[9] 10,000 to < 20,000
[10] 40,000 to < 50,000
[11] $10 million to < $20 million
[12] $20 million to < $30 million
[13] $40 million to < $50 million
[14] $50 million to < $60 million
[15] net cost saving
[16] $0 to < $10 million

11.4 The total net cost to the PBS/RPBS of listing deucravacitinib was estimated to be $0 to < $10 million in Year 6, and a total of $0 to < $10 million in the first 6 years of listing (using effective price for deucravacitinib and the published prices of substituted medicines). The use of the published price for apremilast will overestimate the offsets as it has a special pricing arrangement.

For more detail on PBAC's view, see section 12 PBAC outcome.

12 PBAC outcome

12.1 The PBAC recommended the Authority Required (STREAMLINED) listing of deucravacitinib for the treatment of severe chronic plaque psoriasis (CPP). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of deucravacitinib would be acceptable with an ICER of $30,000 to $45,000/ QALY.

12.2 The PBAC is satisfied that deucravacitinib provides, for some patients, a significant improvement in efficacy over apremilast.

12.3 The PBAC recalled it had previously deferred making a recommendation for deucravacitinib as it was uncertain whether the proposed clinical place of deucravacitinib (in the same line of therapy as apremilast) was reasonable. The PBAC noted some uncertainties remained regarding how deucravacitinib would be used in clinical practice, but considered that, overall, the proposed place in therapy was reasonable and apremilast was the appropriate comparator.

12.4 The PBAC considered it was appropriate for the restriction criteria for deucravacitinib to be consistent with the criteria for apremilast.

12.5 The PBAC noted flow-on changes to the apremilast criteria will be required to preclude concurrent treatment with deucravacitinib and flow-on changes to the bDMARD criteria for severe chronic plaque psoriasis will be required to add deucravacitinib to the list of prior therapies that patients may trial before being eligible for PBS-subsidised biologics.

12.6 The PBAC reiterated its previous consideration that it was appropriate to use the trial-based utilities in the economic model, rather than the Zug utilities (see paragraph **Error! Reference source not found.**). The PBAC noted the ICER using the revised economic model, the revised price of deucravacitinib, the confidential prices of apremilast and adalimumab remained high (see **Error! Reference source not found.**).

12.7 The PBAC advised an additional price reduction of approximately 4% would be required to ensure deucravacitinib is cost-effective for the treatment of CPP. The PBAC considered deucravacitinib would be cost-effective with an ICER of $30,000 to $45,000/QALY. The PBAC noted this is within the ICER range previously accepted for treatments for severe CPP ($15,000 to $45,000/ QALY) (Section 12, ustekinumab PSD, November 2009 PBAC meeting; paragraph 4.7, CPP PMR, July 2020 PBAC meeting).

12.8 The PBAC considered the financial estimates model provided with the proposal was reasonable, but the financial implications of listing need to be revised to incorporate a lower deucravacitinib price. The PBAC noted the financial estimates model assumed cost savings due to reduced use of apremilast and adalimumab (as a proxy for bDMARDs). The PBAC considered it was likely deucravacitinib would replace apremilast in clinical practice given deucravacitinib was more effective. The PBAC considered cost savings due to reduced use of bDMARDs is likely to be realised (at

least initially) as the use of the more costly bDMARDs will be displaced in a proportion of patients.

12.9 The PBAC advised a risk sharing arrangement with expenditure caps based on the revised financial estimates (as outlined in the paragraph above) and a 100% rebate for any use above the caps would be appropriate to manage the uncertainty associated with the utilisation of deucravacitinib.

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

a) The treatment is expected to provide a clinically relevant improvement in efficacy over apremilast; however, the clinical benefit was likely to be modest;
b) The treatment is not expected to address a high and urgent unmet clinical need due to the availability of other treatment options for CPP;
c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

12.11 The PBAC recommended that deucravacitinib should not be treated as interchangeable with any other drugs.

12.12 The PBAC advised that deucravacitinib is not suitable for prescribing by nurse practitioners.

12.13 The PBAC recommended that the Early Supply Rule should apply.

12.14 The PBAC noted that this submission is not eligible for an Independent Review

Outcome:
Recommended

13 Recommended listing

13.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DEUCRAVACITINIB					
Deucravacitinib 6 mg tablet, 28	NEW	1	28	5	Sotyktu®

Restriction Summary [new 1] / Treatment of Concept: [new 2]	
	Category / Program: General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (STREAMLINED) (code: new 2)
	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.
	Episodicity: Chronic
	Severity: Severe
	Condition: Plaque psoriasis
	Indication: Severe chronic plaque psoriasis
	Clinical criteria:
	Patient must not have achieved adequate response after at least 6 weeks of treatment with methotrexate prior to initiating treatment with this drug; OR
	Patient must have a contraindication to methotrexate according to the Therapeutic Goods Administration (TGA) approved Product Information; OR
	Patient must have demonstrated severe intolerance of, or toxicity due to, methotrexate
	AND
	Clinical criteria:
	The condition must have caused significant interference with quality of life.
	AND
	Clinical criteria:
	Patient must not be undergoing concurrent PBS-subsidised treatment for psoriasis with each of: (i) a biological medicine, (ii) ciclosporin; (iii) apremilast
	Treatment criteria:
	Must be treated by a medical practitioner who is either: (i) a dermatologist, (ii) an accredited dermatology registrar in consultation with a dermatologist; OR
	Must be treated by a general practitioner who has been directed to continue treatment (not initiate treatment) by one of the above practitioner types
	Population criteria:
	Patient must be at least 18 years of age

13.2 Flow on changes:

1- to apremilast listing to:

- preclude concurrent treatment with deucravacitinib and replace clinical criterion '*Patient must not be undergoing concurrent PBS-subsidised treatment for psoriasis with each of: (i) a biological medicine, (ii) ciclosporin'* with a new criterion: '*Patient must not be undergoing concurrent PBS-subsidised treatment for psoriasis with each of: (i) a biological medicine, (ii) ciclosporin; (iii) deucravacitinib'*
- replace clinical criterion *'Patient must have failed to achieve an adequate response after at least 6 weeks of treatment with methotrexate prior to initiating treatment with this drug; or'* with new concept '*Patient must not have achieved adequate response after at least 6 weeks of treatment with methotrexate prior to initiating treatment with this drug; or'*

2- to biological medicines for severe chronic plaque psoriasis:

Add deucravacitinib to the list of prior therapies that patients may trial before being eligible for PBS-subsidised biologics. An example of one of the relevant concepts (attached to

etanercept) is reproduced below:

> Patient must have failed to achieve an adequate response, as demonstrated by a Psoriasis Area and Severity Index (PASI) assessment, to at least 2 of the following 5 treatments: (i) phototherapy (UVB or PUVA) for 3 treatments per week for at least 6 weeks; (ii) methotrexate at a dose of at least 10 mg weekly for at least 6 weeks; (iii) ciclosporin at a dose of at least 2 mg per kg per day for at least 6 weeks; (iv) acitretin at a dose of at least 0.4 mg per kg per day for at least 6 weeks; (v) apremilast at a dose of 30 mg twice a day for at least 6 weeks; (vi) *deucravacitinib at a dose of 6 mg once daily for at least 6 weeks.*

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

14 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.

15 Sponsor's Comment

The Sponsor welcomes this recommendation from the PBAC and looks forward to continuing to work with the Department of Health to provide access to deucravacitinib for the treatment of chronic plaque psoriasis (CPP).