An addendum has been included at the end of the minute.

7.04 MOGAMULIZUMAB, Solution concentrate for I.V. infusion 20 mg in 5 mL, Poteligeo®, Kyowa Kirin Australia Pty Ltd.

1 Purpose of submission

1.1 The standard re-entry resubmission requested a Section 100 (Efficient Funding of Chemotherapy Program) listing for the treatment of relapsed or refractory cutaneous T-cell lymphoma (CTCL; mycosis fungoides or Sezary syndrome) previously treated with at least one prior systemic therapy.

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus vorinostat (revised to a cost-minimisation approach (CMA) in the Pre-Sub-Committee Response (PSCR)). The key components of the resubmission are presented in Table 1.

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

Component	Description
Population	CTCL patients with relapsed or refractory mycosis fungoides (MF) or Sezary syndrome (SS)
Intervention	Mogamulizumab 1.0 mg/kg IV weekly on days 1, 8, 15 and 22 of the first cycle, followed by every 2 weeks on days 1 and 15 of each subsequent 28-day cycle until disease progression or unacceptable toxicity.
Comparator	Main: Vorinostat 400 mg orally daily, until disease progression or unacceptable toxicity Secondary: Extracorporeal photopheresis (ECP) with methoxsalen 20 mcg/mL, at a recommended dose of 0.017 mL methoxsalen per mL of ECP treatment volume, on 2 consecutive days per month for 6 months and 1 treatment every 6 weeks thereafter Tertiary: Brentuximab vedotin 1.8 mg/kg IV every 3 weeks, for up to 16 cycles.
Outcomes	PFS, ORR, TTR, DOR, TTNT, OS, HRQoL and safety
Clinical claim	In patients with relapsed or refractory MF or SS, mogamulizumab provides significantly and importantly superior effectiveness with non-inferior safety to vorinostat. No formal claim was made in relation to the comparisons with ECP or brentuximab vedotin

Source: Table 1-1, p13 of the resubmission.
CTCL = cutaneous T-cell lymphoma; DOR = duration of response; ECP = extracorporeal photopheresis; HRQoL = health-related quality of life; IV = intravenous; kg = kilogram; MF = mycosis fungoides; ORR = overall response rate; OS = overall survival; PFS = progression free survival; SS = Sezary syndrome; TTNT = time to next treatment; TTR = time to response.
Blue shading indicates data previously seen by the PBAC.

2 Background

Registration status

2.1 Mogamulizumab was registered by the Therapeutic Goods Administration (TGA) on 5 February 2021 for the following indication: treatment of adult patients (18 years of age and above) with mycosis fungoides (MF) or Sezary syndrome (SS) who have received at least one prior systemic therapy.

Previous PBAC consideration

2.2 Mogamulizumab in the proposed population was considered, and not recommended for listing, by the Pharmaceutical Benefits Advisory Committee (PBAC) at its meetings in July 2020 and November 2020. A summary of the key matters of concern from those previous considerations and how they were addressed in the current resubmission is presented in Table 2.

Table 2: Summary of key matters of concern

Component	Matter of concern	How the resubmission addresses it
Clinical evidence		
Open-label design and high crossover for key trial (MAVORIC)	High risk of bias; potentially subjective mSWAT; uncertain reliability of comparative effectiveness for progression (para 7.4, mogamulizumab, PSD, July 2020 PBAC meeting)	Inadequately addressed. The resubmission introduced an unanchored MAIC examining survival outcomes between mogamulizumab from MAVORIC versus vorinostat from ANCLD.
Impact of crossover on PFS and OS in MAVORIC	High and early crossover confounding PFS and OS interpretation; uncertain treatment effect; median PFS for crossover group longer than either arm (para 7.5, mogamulizumab, PSD, July 2020 PBAC meeting)	
Limitations in crossover adjustments applied to adjust OS in MAVORIC	None of the methods used for the crossover adjustments resulted in statistically significant hazard ratios for OS; 73.1% crossed over early; unlikely that any of the methods applied to adjust OS for treatment switching could obtain valid estimates for the incremental benefit of mogamulizumab over vorinostat (para 7.6, mogamulizumab, PSD, July 2020 PBAC meeting)	
Inconsistent vorinostat ORR	Substantially lower ORR of vorinostat in MAVORIC vs. its older trials; differences in response definitions and treatment duration; uncertain link to survival or QoL (para 6.5, mogamulizumab, PSD, November 2020 PBAC meeting)	Not addressed.
Economic evaluation		
Time horizon	The model horizon of 20 years was considered long (para 6.56, mogamulizumab PSD, July 2020 PBAC Meeting)	The time horizon was reduced to 10 years.

Component	Matter of concern	How the resubmission addresses it
Clinical benefit	The PBAC considered the extent of benefit for mogamulizumab versus vorinostat could not be determined from the available evidence in MAVORIC (para 7.7, mogamulizumab PSD, July 2020 PBAC Meeting) and advised that a cost-utility analysis may not be an appropriate method to determine the cost effectiveness of mogamulizumab based on the data presented (para 7.10, mogamulizumab PSD, July 2020 PBAC Meeting). No additional clinical trial data were presented to inform the clinical claims of the minor submission in November 2020. As such, the PBAC reaffirmed its July 2020 advice, that the extent of benefit, if any, for mogamulizumab versus vorinostat could not be determined from the available evidence (para 6.6, mogamulizumab PSD, November 2020 PBAC Meeting).	The additional evidence presented by the resubmission did not adequately support the claim of superior effectiveness of mogamulizumab versus vorinostat.
Quality of life	The ESC noted that the utility values from MAVORIC were estimated based on the UK tariffs rather than the Australian specific tariffs (para 6.62, mogamulizumab PSD, July 2020 PBAC Meeting).	Unchanged.
Requested effective AEMP for one vial	$[redacted] in July 2020 and $[redacted] in November 2020.	$[redacted].
ICER	$[redacted][1]/QALY in July 2020 submission. The PBAC considered the ICER unacceptably high and uncertain (para 7.10, mogamulizumab PSD, July 2020 PBAC Meeting). $[redacted][2]/responder in November 2020 submission (corrected to $[redacted][3] during the evaluation) - the PBAC considered the ICER was unacceptably high (para 6.8, mogamulizumab PSD, November 2020 PBAC Meeting)	The ICER ($[redacted][1]/QALY) was somewhat lower than that in the July 2020 submission. The PSCR (p1) proposed a CMA.

AEMP = approved ex-manufacturer price; ANCLD = Australian National Cutaneous Lymphoma Database; CMA = cost-minimisation approach; CUA = cost-utility analysis; DUSC = Drug Utilisation Sub Committee; ICER = incremental cost effectiveness ratio; MAIC = matching-adjusted indirect comparison; mSWAT = Modified Severity-Weighted Assessment Tool; PBAC = Pharmaceutical Benefits Advisory Committee; PFS = progression-free survival; PSD = Public Summary Document; ORR = overall response rate; OS = overall survival; QALY = quality-adjusted life years; QoL = quality of life.

The redacted values correspond to the following ranges:

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

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

[3] *$255,000 to < $355,000*

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

3 Requested listing

MEDICINAL PRODUCT Form	Dispensed Price Max Amt	Max. Amount	№.of Rpts
Initial treatment			
MOGAMULIZUMAB	PUBLISHED $15,060.13 (Public hospital) $15,314.38 (Private hospital) EFFECTIVE PRICE $[redacted] (Public hospital) $[redacted] (Private hospital)	120 mg	7
Continuing treatment			
MOGAMULIZUMAB	PUBLISHED $15,060.13 (Public hospital) $15,314.38 (Private hospital) EFFECTIVE $[redacted] (Public hospital) $[redacted] (Private hospital)	120 mg	5
Available brands			
Poteligeo (mogamulizumab 20 mg/5 mL injection, 5 mL vial)			

Source: Table 1-3 and Table 1-4, p26 of the resubmission.

Category / Program: Section 100 – Efficient Funding of Chemotherapy (Public/Private hospital)
Prescriber type: ☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐
Restriction type: ☒ Authority Required – delayed/non-real time assessment by Services Australia (written application lodged by mail or electronic upload)
Condition: Cutaneous T-cell lymphoma
Indication: Cutaneous T-cell lymphoma
Treatment Phase: Initial treatment
Clinical criteria:
Patient must have a histologically confirmed diagnosis of mycosis fungoides; or
Patient must have a histologically confirmed diagnosis of Sezary syndrome
AND
Clinical criteria:
Patient must have experienced a relapse or is refractory to a prior systemic therapy for this condition;
AND
Clinical criteria:
The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition.
Prescribing Instructions: Applications for authorisation of initial treatment must be in writing and must include: (a) a completed authority prescription form; and (b) a completed cutaneous T-cell lymphoma (CTCL) initial PBS Authority Application - Supporting Information Form
Administrative Advice: Special Pricing Arrangements apply.

Category / Program: Section 100 – Efficient Funding of Chemotherapy (Public/Private hospital)
Prescriber type: ☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐
Restriction type: ☒ Authority Required - immediate/real-time assessment by Services Australia (telephone / online emergency)
Condition: Cutaneous T-cell lymphoma
Indication: Cutaneous T-cell lymphoma
Treatment Phase: Continuing treatment
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition.
AND
Clinical criteria:
Patient must not have progressive disease while receiving PBS-subsidised treatment with this drug for this condition.
AND
Clinical criteria:
The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition.
Prescribing Instructions: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).
Administrative Advice: Special Pricing Arrangements apply.

Source: Table 1-5, p26 of the resubmission.

3.1 The resubmission proposed a special pricing arrangement (SPA) with a published ex-manufacturer price (EMP) of $2,495 per vial and an effective EMP of $ per vial. The proposed price was % lower than that offered in the July 2020 submission ($ per vial) and % lower than in the November 2020 resubmission ($ per vial). The PSCR proposed a CMA which resulted in a revised EMP of $ per vial.

3.2 The ESC noted the PSCR proposed a CMA to vorinostat and considered it would be reasonable to align the restriction for mogamulizumab with the current vorinostat restriction for cutaneous T cell lymphoma, including:

- Adding the clinical criteria 'Patient must be ineligible for stem cell transplant'. The ESC acknowledged that this was not a requirement for the MAVORIC trial but advised that in clinical practice a stem cell transplant (SCT) would be used in preference to mogamulizumab if indicated;
- Removing the clinical criteria 'Patient must have a histologically confirmed diagnosis of mycosis fungoides' or 'Patient must have a histologically confirmed diagnosis of Sezary syndrome';
- Replacing the clinical criteria 'Patient must have experienced a relapse or is refractory to a prior systemic therapy for this condition' with the 'Patient must have received systemic treatment with chemotherapy' and 'Patient must demonstrate relapsed or chemotherapy-refractory disease; and
- Replacing the clinical criteria 'The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition' with 'The treatment must be the sole PBS-subsidised therapy for this condition'.

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

4 Population and disease

4.1 CTCL is a rare subtype of non-Hodgkin lymphoma (2-3% of cases) that presents with skin manifestation at diagnosis and eventually involves the lymph nodes, blood and internal organs. The two most common forms of CTCL are MF or SS which comprise approximately two-thirds of CTCL cases, with MF representing the majority of these in most treatment settings. All CTCL subtypes are defined by abnormal clonal proliferations of mature T-cells that infiltrate the skin and eventually manifest into patches, plaques, tumours, and/or erythroderma. MF is characterised by an aggressive disease state and is associated with poor survival. SS is an advanced and severe disease state with a historical median survival of less than 3 years. In Australia, the incidence rate of MF is estimated at 0.30 per 100,000 persons per year, with 93 new cases reported in 2020. SS is much rarer, with only 8 cases reported in the same year (Australian Institute of Health and Welfare; AIHW). The incidence of CTCL increases significantly with age, with a median age at diagnosis of around 55 years and a 4-fold increase in incidence in patients over 70 years.

4.2 Mogamulizumab is a defucosylated, humanised immunoglobulin G (IgG1) kappa immunoglobulin that selectively binds to C-C chemokine receptor 4 (CCR4), a G-protein-coupled receptor for CC chemokines that is involved in the trafficking of lymphocytes to various organs including the skin. CCR4 is expressed on the surface of some T cell malignancies, such as MF and SS as well as Type 2 T helper (Th2) T cells and regulatory T cells (Tregs). Binding of mogamulizumab to CCR4 induces antibody-dependent cellular cytotoxicity (ADCC), resulting in the depletion of target cells.

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

5 Comparator

5.1 The resubmission nominated vorinostat as the main comparator, with extracorporeal photopheresis (ECP) combined with methoxsalen and brentuximab vedotin (brentuximab) as the secondary and tertiary comparators, respectively. The PBAC previously accepted vorinostat as the main comparator and brentuximab as the secondary comparator in its July 2020 consideration of mogamulizumab (para 7.3, mogamulizumab, Public Summary Document (PSD), July 2020 PBAC meeting). The resubmission did not include evidence of cost-effectiveness for mogamulizumab against ECP or brentuximab but included both as cost-offsets in the financial estimates. The ESC noted that ECP in combination with methoxsalen targets a different aspect of disease management to mogamulizumab. The ESC considered the nomination of vorinostat as the main comparator was appropriate.

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

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6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinicians presented clinical case studies describing the impact of CTCL on patients. The clinicians noted that patients often had very poor quality of life due to the burden of skin related symptoms such as plaques, tumours, erythroderma, scales, extensive itching and skin pain. Such symptoms often affect patients hands and feet making it difficult for them to function. The clinicians described an unmet need for new treatments as remissions were short with no patients cured of the disease. The clinicians outlined the limitations associated with the treatment options currently available and highlighted the unique mechanism of action of mogamulizumab. Mogamulizumab was described as being a well-tolerated short infusion, with infusion reactions rare (primarily skin rashes). The clinicians considered mogamulizumab had a high response rate and would be particularly useful in patients with blood compartment involvement. The PBAC considered that the hearing was informative as it provided a clinical perspective on treating this uncommon disease.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (15), health care professionals (7) and organisations (2) via the Consumer Comments facility on the PBS website. The comments from health care professionals described the high symptom burden often faced by patients with relapsed or refractory CTCL and highlighted that durable remissions are not attained with one line of treatment. Health care professionals emphasised the importance of treatments to improve disease control and quality of life and said that this was as important as survival outcomes which are difficult to assess in this condition. Health care professionals also highlighted the benefit for patients in rural or regional centres who could potentially be administered mogamulizumab at community-based hospitals with Telehealth services to access expert medical care in major city hospitals. The input from individuals with the condition and from those involved in directly caring for an individual with the condition described the debilitating nature of CTCL including fatigue and the significant impact of skin symptoms (such as red, angry and itchy skin) that causes great discomfort and anxiety, as well as social isolation. The comments from individuals with the condition described the side effects associated with current treatment options. The comments also noted cost as a barrier and the difficulty in accessing current treatments for those living in regional or remote areas. All comments, including those from the Leukaemia Foundation and Rare Cancers Australia highlighted the need for new treatment options in the management of this rare cancer.

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Clinical studies

6.3 The resubmission was based on an unanchored matching-adjusted indirect comparison (MAIC) between mogamulizumab and vorinostat. The unanchored MAIC examined overall survival (OS) outcomes by utilising individual patient data from mogamulizumab in MAVORIC, matched to summary-level data for vorinostat from the ANCLD (Australian National Cutaneous Lymphoma Database) study.

6.4 MAVORIC (N = 372) was the pivotal trial for mogamulizumab presented in the July 2020, November 2020 and current March 2025 (re)submissions. The ANCLD study (N = 64) was an analysis of patients receiving vorinostat at the Peter MacCallum Cancer Centre in Melbourne Australia, conducted in August 2020. This is the first time data from the ANCLD have been presented to the PBAC in support of a listing for mogamulizumab. The unanchored MAIC was performed by matching patients based on sex and CTCL subtypes.

6.5 The resubmission did not provide a clear justification for the choice of outcome (OS) and the source of data used for the comparator (ANCLD report) used in the MAIC. Specifically, the resubmission noted that while the ANCLD report includes time to next treatment (TTNT) outcomes, no comparison of TTNT was conducted in the MAIC, citing potential bias due to differential access to subsequent therapies between the respective clinical trial and real-world settings. However, no additional evidence was provided to justify excluding TTNT from the MAIC. TTNT could have been included as an additional endpoint in a sensitivity analysis. In addition, other sources such as Study P001 and Study P005 which formed the basis of the March 2017 recommendation for vorinostat listing on the PBS (para 6.12, brentuximab vedotin PSD, July 2018 PBAC Meeting) could have provided data for overall response rate (ORR) and progression-free survival (PFS) outcomes of vorinostat for an unanchored MAIC.

6.6 Details of the studies presented in the resubmission are provided in Table 3.

Table 3: Key studies and associated reports presented in the resubmission

Study identifier (ID)	Reports	Publication citation
MAVORIC KW-0761-010 NCT01728805	Clinical Study Report: Open-label, Multi-center, Randomised Study of Anti-CCR4 Monoclonal Antibody KW-0761 (mogamulizumab) Versus Vorinostat in Subjects with Previously Treated Cutaneous T-cell Lymphoma (CTCL) Supplementary Report: Quality of Life Analysis in Subjects with Cutaneous T-Cell Lymphoma Treated with Anti-CCR4 Monoclonal Antibody KW-0761 (Mogamulizumab) Versus Vorinostat; (1 August 2017). Key publication: Kim Y, Bagot M, Pinter-Brown L, al e. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial.	August 2017 August 2017 *Lancet Oncol*. 2018;19 (9):1192-1204
ANCLD study	Unpublished report: Vorinostat analysis of Peter Mac Cutaneous Lymphoma database	August 2020
Unanchored matching-adjusted indirect comparison (unanchored MAIC) report/ Remak et al., 2021	MAIC Report/ Remák E, Hawkins N, Jones T, Otley M, Twigger R, Prince M. Understanding relative survival outcomes for patients with cutaneous T-cell lymphoma (CTCL) subtypes mycosis fungoides and Sézary syndrome treated with mogamulizumab or vorinostat: Combining Australian real-world evidence and MAVORIC phase 3 trial data.	European Journal of Cancer. 2021 Oct 1;156:S18.

Source: Table 2-1, pp34-36 of the resubmission.
Blue shading indicates data previously seen by the PBAC.

6.7 The key features of the key studies are summarised in Table 4.

Table 4: Key features of the key evidence

Study	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
Mogamulizumab: RCT (versus vorinostat)						
MAVORIC	372	R, OL/17 months	High	MF or SS ≥ 1 prior systemic therapy	PFS, ORR, DOR, OS, TTF, TTR, HRQoL, AEs, TTNT	HRQoL
Vorinostat: Non-randomised studies						
ANCLD study	64	Retrospective/NR	High	MF or SS receiving vorinostat	OS, TTNT	-
Indirect comparison (mogamulizumab versus vorinostat)						
Unanchored-MAIC	186 (mogamulizumab) 64 (vorinostat)	Included MAVORIC and ANCLD; assessed OS				OS

Source: p53 of the March 2025 resubmission; Table 3, mogamulizumab, PSD, July 2020 PBAC meeting.
AEs = adverse events; ANCLD = Australian National Cutaneous Lymphoma Database; DB = double blind; DOR = duration of response; HRQoL = health-related quality of life; MAIC = matching-adjusted indirect comparison; MC = multi-centre; MF = mycosis fungoides; NR = not reported; OL = open label; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; R = randomised; SS = Sezary syndrome; TTF = time to treatment failure; TTNT = time to next treatment; TTR = time to response.
Blue shading indicates data previously seen by the PBAC.

6.8 At its July 2020 meeting the PBAC was of the view, which it reaffirmed at its November 2020 meeting, that MAVORIC had a high risk of bias due to its open label design and extent of crossover (para 5.4, mogamulizumab, PSD, November 2020 PBAC meeting).

Specifically, the high and early crossover in MAVORIC from vorinostat to mogamulizumab confounded the interpretation of PFS and OS outcomes (para 7.5 and para 7.6, mogamulizumab, PSD, July 2020 PBAC meeting). The PBAC also considered that none of the crossover adjustment analyses presented in the July 2020 submission could provide valid estimates for the incremental benefit of mogamulizumab over vorinostat (para 7.6, mogamulizumab, PSD, July 2020 PBAC meeting). The PBAC further considered that comparative data on ORR from MAVORIC was uncertain, particularly due to the impact of the short duration of treatment with vorinostat in MAVORIC (para 6.5, mogamulizumab, PSD, November 2020 PBAC meeting). The current resubmission did not address these specific concerns (and the comparative data presented from MAVORIC remained unchanged from the July 2020 submission).

6.9 The risk of bias of the ANCLD study was considered high primarily due to its non-randomised design and retrospective nature. The ANCLD study reported limited baseline characteristics for patients, and data on key prognostic factors at treatment initiation, such as Eastern Cooperative Oncology Group (ECOG) performance status and disease stage, were not available. This absence of data limits the ability to assess patients' overall health and disease severity when they started receiving vorinostat.

6.10 There is limited information on the baseline characteristics of patients available from both MAVORIC and ANCLD that were used to inform the unanchored MAIC. Specifically, patients in ANCLD differed from those in MAVORIC in terms of:

- Having a higher number of prior therapies (5), compared to MAVORIC (3).
- Having a higher percentage of females (52%), compared to MAVORIC (41%).
- Having a lower percentage of prior treatment with ECP (27%) and psoralen plus ultraviolet A therapy (PUVA; 17%), compared to MAVORIC (38% for ECP, and 43% for PUVA).

Additionally, MAVORIC applied stringent eligibility criteria, excluding participants with various comorbidities and those considered unfit, including those with large cell transformation—a critical prognostic factor associated with poor outcomes in CTCL. However, ANCLD applied no criteria in its selection of patients for analysis, including all patients who received vorinostat from the Peter MacCallum Cancer Centre regardless of their baseline health status. Specifically, ANCLD is likely to include a substantial proportion of patients with advanced disease stages, as suggested by skin scores at treatment initiation (47% of T4, and 70% of T3 to T4). In contrast, MAVORIC included a high proportion of mogamulizumab patients with good performance status, as indicated by ECOG scores (57% with a score of 0 and 98.9% between 0 to 1), reflecting a predominantly healthier or less functionally impaired population at baseline. Collectively, ANCLD may have included patients with more severe disease than those in MAVORIC.

Comparative effectiveness

6.11 PFS was the primary outcome in MAVORIC, and the results in the resubmission remain unchanged from those previously seen by the PBAC.

6.12 OS outcomes from MAVORIC were exploratory. A summary of OS outcomes between mogamulizumab and vorinostat in MAVORIC per its Clinical Study Report (CSR) with a data cut-off of 31 December 2016 previously seen by the PBAC is presented in Table 5. As in previous submissions, the OS results from MAVORIC were also reported with analyses from later cut-off dates, including an analysis with a data cut-off of 2 March 2019, and another analysis with the same cut-off date that excluded patients with SCT. The resubmission did not specify which OS results were used to inform the MAIC for mogamulizumab.

Table 5: Overall survival between mogamulizumab versus vorinostat in MAVORIC

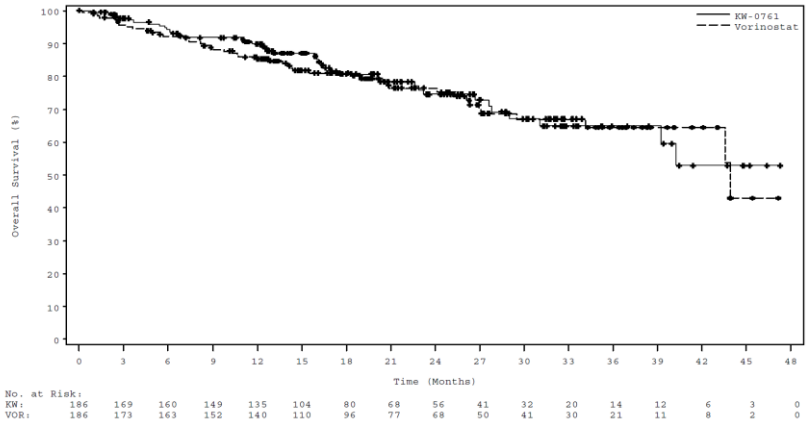
	Mogamulizumab (N=186)	Vorinostat (N=186)	Absolute difference	HR (95% CI)
Overall survival				
Deaths, n/N (%)	40/186 (21.5)	47/186 (25.3)	-	0.93 (0.61, 1.43)
Median months OS (95% CI)	-	43.93 (43.57, -)	NE	p-value = 0.9439
% alive at 6 months (95% CI)	94.2 (89.5, 96.9)	92.3% (87.3, 95.4)	1.9	-
% alive at 12 months (95% CI)	89.9 (84.3, 93.6)	85.3 (79.2, 89.8)	4.6	-
% alive at 18 months (95% CI)	80.7 (73.0, 86.4)	81.0 (74.2, 86.2)	-0.3	-
% alive at 24 months (95% CI)	74.6 (65.6, 81.6)	76.4 (68.6, 82.5)	-1.8	-
% alive at 30 months (95% CI)	67.1 (56.0, 76.0)	67.0 (57.2, 75.1)	0.1	-
% alive at 36 months (95% CI)	65.0 (53.3, 74.4)	64.5 (53.8, 73.4)	0.5	-
% alive at 42 months (95% CI)	52.9 (34.3, 68.5)	64.5 (53.8, 73.4)	11.6	-

Source: Table 2-49, p107 of the March 2025 resubmission.
CI = confidence interval; n = number of participants with event; N = total participants in group
Blue shading indicates data previously seen by the PBAC.

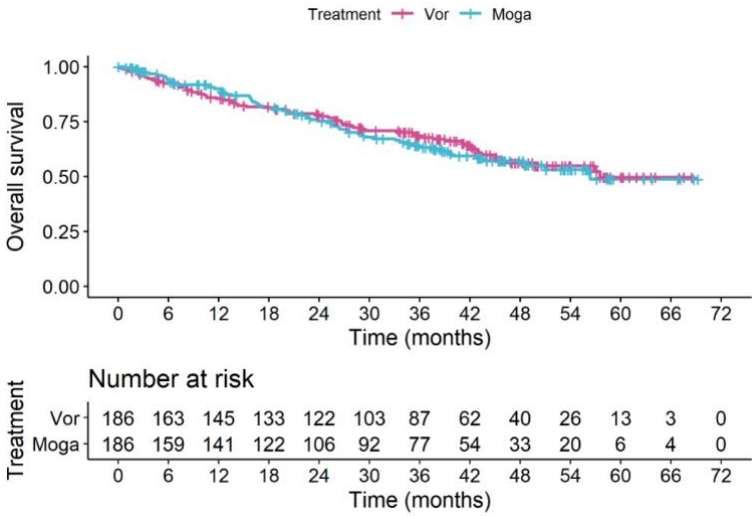
6.13 The Kaplan Meier (KM) plots of OS between mogamulizumab and vorinostat in MAVORIC from cut-off dates of 31 December 2016 (above) and 2 March 2019 (below) are presented in Figure 1.

Figure 1: Kaplan-Meier curve of overall survival of mogamulizumab (versus vorinostat) in MAVORIC

A (31 December 2016 cut-off date)



B (2 March 2019 cut-off date)



Source: Figure 2-18, p107; Figure 2-21, p111 of the resubmission.
CI = confidence interval; SCT = stem cell transplant; n = number of events, N = number of participants; NA = not applicable
Note: Patients in MAVORIC were recruited between 12 December 2012 and 29 January 2016.

6.14 A summary of OS of vorinostat in ANCLD is presented in Table 6.

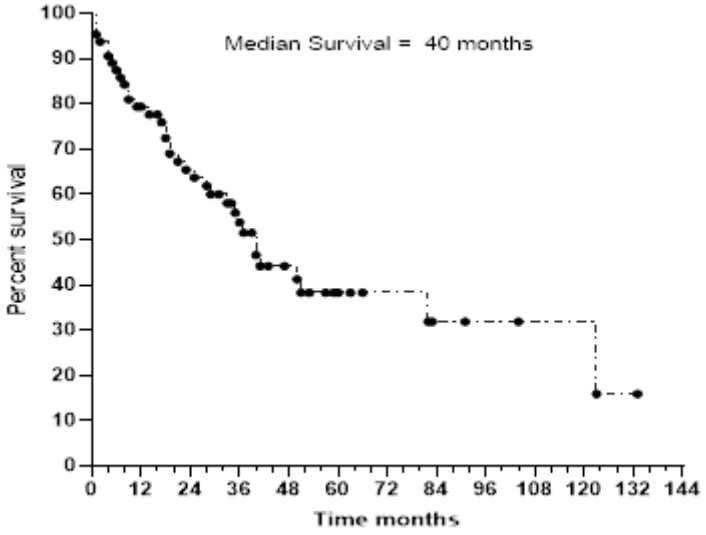
Table 6: Overall survival of patients receiving vorinostat in ANCLD

	Vorinostat (N=64)
Median OS, months (95% CI)	40 (29.0, 81.9)
Deaths, n/N (%)	29/64 (45.3%)

Source: Table 2-87, p151 of the resubmission; pp13-14 of the ANCLD report
ANCLD = Australian National Cutaneous Lymphoma Database; CI = confidence interval; n = number of participants with event; N = total participants in group; OS = overall survival.

6.15 The KM plot of OS of vorinostat from ANCLD is presented in Figure 2.

Figure 2: Overall survival from initiation of vorinostat from ANCLD



Source: Figure 2-32, p131 of the resubmission.
ANCLD = Australian National Cutaneous Lymphoma Database

6.16 A summary of the results from the unanchored MAIC is presented in Table 7.

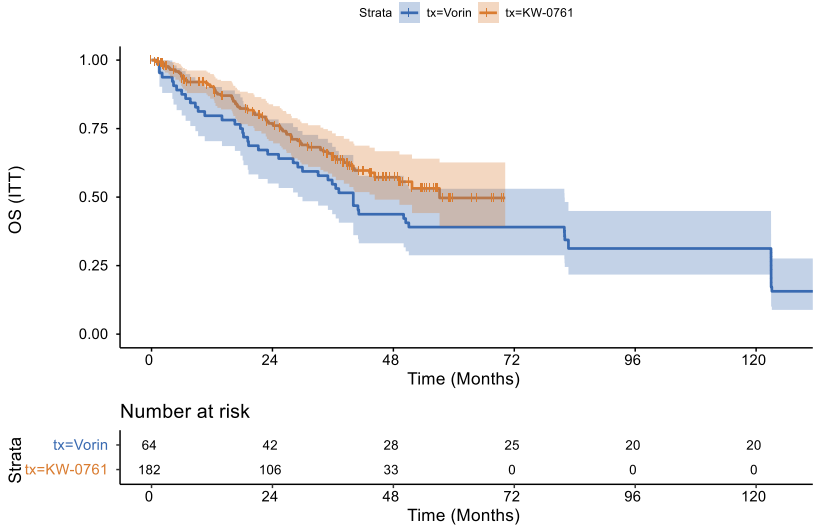
Table 7: Summary of OS outcomes from the unanchored MAIC

	Before matching		Matching adjusted indirect comparison	
	Mogamulizumab, MAVORIC (n=186)	**Vorinostat, ANCLD (n=64)**	**Mogamulizumab, MAVORIC (n=182)**	**Vorinostat, ANCLD (n=64)**
Median OS (95% CI)	Not reported	40.0 (29.0-81.9)	57.2 (44.3-NR)	40.0 (29.0-81.9)
Hazard ratio (95% CI)	Not reported		0.68 (0.45, 1.02)	
p-value	Not reported		0.06	

Source: Figure 2-32, p131; Table 2-87, p151 of the resubmission.
ANCLD = Australian National Cutaneous Lymphoma Database; CI = confidence interval; MAIC = matching-adjusted indirect comparison; N = number of participants; NR = not reported.

6.17 The KM curves of the OS outcome from the MAIC results are presented in Figure 3.

Figure 3: Kaplan-Meier analysis of overall survival from the unanchored MAIC



Source: Figure 2-46, p151 of the resubmission.
ITT = intention-to-treat; KW-0761 = mogamulizumab, MAIC = matching-adjusted indirect comparison; OS = overall survival; tx = treatment; Vorin = vorinostat

6.18 The ESC noted the results from the MAIC suggest a numerical improvement in OS for mogamulizumab compared to vorinostat (hazard ratio = 0.68; p-value = 0.06), but the difference was not statistically significant. The wide confidence interval (95% CI 0.45, 1.02) indicates uncertainty in the estimate.

6.19 The evaluation and the ESC considered the MAIC was inadequately conducted, primarily due to a lack of robust data. Specifically, the matching adjustment between MAVORIC and ANCLD was based only on two prognostic variables: sex and CTCL subtypes. Other critical prognostic variables (e.g., disease stage and large cell transformation) and treatment effect modifiers were not included in the matching process due to the absence of data from either MAVORIC or ANCLD. Given the likely differing baseline characteristics between the two datasets (see paragraph 6.10), this inadequate matching adjustment likely resulted in unmeasured confounding and bias in the comparative outcome. Overall, the evaluation and the ESC considered the results from the MAIC to be unreliable. However, based on the results of the clinical data submitted, the ESC considered it would be reasonable to conclude that mogamulizumab is non-inferior in effectiveness to vorinostat.

Comparative harms

6.20 No additional comparative safety data for mogamulizumab versus the proposed comparators beyond what has previously been seen by the PBAC were provided by the March 2025 resubmission. At its July 2020 meeting, the PBAC noted that the incidence of drug-related adverse events (AEs) and drug-related Grade ≥ 3 AEs was lower in the mogamulizumab arm compared to the vorinostat arm (para 6.41, mogamulizumab, PSD, July 2020, PBAC meeting). However, the PBAC noted a higher incidence of any serious adverse events (SAEs) and treatment-emergent SAEs in the

mogamulizumab arm. Considering these findings, the PBAC considered that the claim of non-inferior comparative safety of mogamulizumab versus vorinostat was reasonable (para 7.8, mogamulizumab, PSD, July 2020, PBAC meeting). The PBAC reaffirmed its July 2020 advice regarding the non-inferior comparative safety claim at its November 2020 meeting (para 6.6, mogamulizumab, PSD, November 2020, PBAC meeting).

Benefits/harms

6.21 The indirect comparison presented did not support the superiority claim. Accordingly, a benefits/harms table has not been presented.

Clinical claim

6.22 The resubmission described mogamulizumab as superior in terms of effectiveness compared to vorinostat. The evaluation and the ESC considered this claim was not supported by the evidence presented. The ESC noted the matching adjustment process used did not adequately incorporate critical prognostic factors and treatment effect modifiers. The ESC also noted that the results of the MAIC suggested that the difference in OS between the treatments was not statistically significant (hazard ratio = 0.68; 95% confidence interval = 0.45, 1.02; p = 0.06). Overall, the ESC considered it reasonable to conclude that mogamulizumab is non-inferior in effectiveness compared to vorinostat.

6.23 The resubmission described mogamulizumab as non-inferior in terms of safety compared to vorinostat. This claim was previously accepted (see paragraph 6.20).

6.24 No formal claim was made for mogamulizumab against ECP and brentuximab. The comparative effectiveness of mogamulizumab versus ECP and brentuximab remains unknown.

6.25 The PBAC considered that the claim of significant and superior clinical effectiveness versus vorinostat was not supported by the data. The PBAC considered a claim of non-inferior comparative effectiveness would be reasonable.

6.26 The PBAC considered that the claim of non-inferior comparative safety versus vorinostat was reasonable, noting that it had considered that this claim was reasonably supported by the data at its July 2020 meeting (paragraph 7.7, mogamulizumab PBAC PSD, July 2020 PBAC Meeting), and that no additional clinical trial data were presented.

Economic analysis

6.27 The resubmission presented a cost-utility analysis (CUA) comparing mogamulizumab with vorinostat. The evaluation considered the evidence presented in the clinical section did not substantiate the claim of superior efficacy of mogamulizumab compared with vorinostat. The evaluation considered a cost-minimisation approach (CMA) comparing mogamulizumab against vorinostat would have been more suitable in this context. Acknowledging the limitations of the clinical data, the PSCR presented

a CMA for mogamulizumab versus vorinostat. As the PSCR presented a CMA, the information provided by the evaluation on the CUA has been removed from the minutes.

6.28 The CMA presented in the PSCR for mogamulizumab versus vorinostat was based on drug costs only (see Table 8). The PSCR proposed the following steady state equi-effective dosing over a 28 day cycle:

- 400 mg vorinostat administered orally daily
- 80 mg of mogamulizumab administered IV on days 1 and 15 only.

As a result of the CMA the PSCR proposed a reduced effective price for mogamulizumab of $[redacted] per vial.

Table 8: Cost-minimisation approach presented in the Pre-Sub-Committee Response

Vorinostat		Mogamulizumab	
Pack quantity (mg)	12,000	Ex-manufacturer cost per 20 mg vial	$[redacted]
Daily dose (mg)	400	Vials per administration	4
Compliance	100%	Average cost/patient/treatment	$[redacted]
Days/pack	30	Treatments per 28 days	2
AEMP/pack	$4,087.01	Compliance	100%
AEMP/day	$136.23	Cost per 28 days	$[redacted]
AEMP per 28 days	$3,814.54		

Source: Table 1, Pre-Sub-Committee Response.

6.29 The ESC noted the CMA used steady-state equi-effective doses over a 28-day cycle. Administration of mogamulizumab on day 1 and 15 of every 28-day cycle was consistent with steady-state per-protocol dosing in MAVORIC and in the TGA Product Information (only the first 28-day treatment cycle required more frequent dosing). The ESC noted that the equi-effective dose assumed 4 x 20 mg vials of mogamulizumab, based on the mean patient weight in MAVORIC of 78.96 kg and the TGA Product Information recommended dose of 1 mg/kg per infusion. The ESC noted that vorinostat dosing was not based on weight and that the equi-effective dose proposed (400 mg per day) was consistent with the per-protocol dosing in MAVORIC and the TGA Product Information.

6.30 In claiming that the equi-effective doses are based on steady-state dosing over a 28-day cycle the resubmission assumed the treatment duration for mogamulizumab and vorinostat would be the same. The ESC noted that the mean treatment durations in MAVORIC were 9.1 cycles for mogamulizumab and 5.4 cycles for vorinostat. However, the ESC recalled the July 2020 PBAC advice that the shorter duration for vorinostat may have been a result of the high and early degree of one-way crossover from vorinostat to mogamulizumab in the trial (para 7.5, mogamulizumab, PSD, July 2020 PBAC meeting). In addition, the ESC considered that evidence from ANCLD indicated that the treatment duration of vorinostat may be longer in clinical practice than evident in MAVORIC. The median duration of treatment with vorinostat reported in ANCLD of 5 months was higher than the median reported in MAVORIC of 3 cycles of 28-days. The ESC also noted that evidence from non-randomised studies indicated the

duration of treatment with mogamulizumab and vorinostat could be similar (median treatment duration of 5 months for vorinostat reported in ANCLD and 4.6 months for mogamulizumab in Beylot-Barry 2023). Overall, the ESC considered the likely treatment duration of mogamulizumab compared to vorinostat in clinical practice to be uncertain, but that it might be reasonable to assume the same treatment duration given the data available.

6.31 The ESC noted that the CMA did not include loading dose or drug administration costs for mogamulizumab and made no adjustment for dose intensity despite MAVORIC reporting a mean dose intensity of 94.41% for mogamulizumab and 88.96% for vorinostat. The ESC considered dosing based on steady-state was reasonable but advised the CMA should be adjusted to include the impact of drug administration costs and differences in dose intensity on the cost of treatment. The ESC also noted that the CMA had not included costs for AEs but considered the nature of the AEs reported was not substantially different between mogamulizumab and vorinostat. The ESC considered the revised CMA outlined in Table 9 which assumed equal treatment duration, adjusted for the mean dose intensity of mogamulizumab and vorinostat in MAVORIC and included the cost of administration of mogamulizumab was appropriate.

Table 9: Revised cost-minimisation approach including adjustment for dose intensity and cost of administration

Vorinostat		Mogamulizumab	
Pack quantity (mg)	12,000	Ex-manufacturer cost per 20 mg vial	$[redacted]
Daily dose (mg)	400	Vials per administration	4
Days per pack	30	MBS cost per administration (item 13950)	$123.05
Dose intensity	88.96%	Dose intensity	94.41%
AEMP/pack	$4,087.01	Average cost/patient/treatment	$[redacted]
AEMP/day	$136.23	Treatments per 28 days	2
AEMP per 28 days	$3,814.54		
Cost per 28 days adjusted for dose intensity	$3,393.42	Cost per 28 days	[redacted]

Source: Compiled in preparation of the ESC Advice.
AEMP = approved ex-manufacturer price; MBS = Medicare Benefits Schedule

6.32 A sensitivity analyses using the revised CMA approach outlined in Table 9 along with the treatment duration in MAVORIC is presented in Table 10.

Table 10 Revised cost-minimisation approach sensitivity analysis

	Treatment duration (28-day cycles)		AEMP per vial (20 mg)
Assumptions	Vorinostat	Mogamulizumab	
Base case (same treatment duration)	Same as mogamulizumab	Same as vorinostat	$[redacted]
MAVORIC mean treatment duration	5.4 cycles	9.1 cycles (18.2 infusions)	$[redacted]
MAVORIC mean treatment duration including mogamulizumab loading dose	5.4 cycles	9.1 cycles (20.2 infusions)	$[redacted]
MAVORIC mean treatment duration for vorinostat applied and mogamulizumab loading dose included	5.4 cycles	5.4 cycles (12.8 infusions)	$[redacted]

Source: Compiled in preparation of the ESC Advice
AEMP = approved ex-manufacturer price

Drug cost/patient

6.33 The PSCR proposed a CMA which resulted in a revised EMP of $[redacted] per vial. The drug cost per patient based on the revised effective price proposed for mogamulizumab in the PSCR is summarised in Table 11.

Table 11: Drug cost per patient for mogamulizumab and vorinostat based on the revised effective price for mogamulizumab proposed in the Pre-Sub-Committee Response

	Mogamulizumab			Vorinostat		
	Trial dose and duration (MAVORIC)	**CMA**	**Financial estimates**	**Trial dose and duration (ANCLD)**	**CMA**	**Financial estimates**
Mean dose intensity	94.41%	100%	100%	NR	100%	100%
Mean duration	19.10 infusions	Not included	20 infusions[b]	21.73 weeks[c]	Not included	5.07 (30-day scripts)[d]
Cost (AEMP)	$[redacted] (per infusion)[a]	$[redacted] (per infusion)[a]	$[redacted] (per infusion)[a]	$953.64 (per week)	$4,087.01 (per 30-day pack) = $1907.27 every 2 weeks	$4,087.01 (per pack)
Cost/patient (AEMP)	$[redacted]	-	$[redacted]	$20,722.59	-	$20,721.14

Source: Table 12.1.1-1 p167-168 of the CSR; Section 3 workbook; Section 4 workbook; Table 1 p3, ANCLD Report
ANCLD = Australian National Cutaneous Lymphoma Database
Note: cost/patient/year = mean dose intensity x mean duration x cost (per infusion or per week or per 30-day script)
a. Assuming 4 x 20 mg vials
b. Mean TOT = 35 weeks; This approximates to 20 scripts (5 scripts for first 5 weeks, then 15 scripts for the 30 subsequent weeks) x 100% dose intensity to produce 20 scripts
c. Assuming median treatment duration in ANCLD (5 months)
d. Assuming median treatment duration in ANCLD (21.73 weeks): 152.11/30

6.34 The mean treatment duration for mogamulizumab used for the financial estimates in the resubmission was based on the average time on treatment reported in MAVORIC (35 weeks: 20 infusions). This was lower than that reported in the July 2020 submission (24.89 infusions), which was based on the average time on treatment estimated from the economic evaluation model at that time (45 weeks; para 6.68, mogamulizumab PSD, July 2020 PBAC Meeting).

6.35 At the revised effective price proposed in the PSCR, the treatment cost per patient per infusion of mogamulizumab was estimated to be $[redacted]. The revised effective price assumed steady-state doses with one infusion every 2 weeks. This differed from the cost per patient based on the trial and assumed in the financial estimates, which incorporate the cost of one infusion every 4 weeks, followed by one infusion every 2 weeks thereafter.

Estimated PBS usage & financial implications

This resubmission was not considered by DUSC. The resubmission used a market share approach to estimate the financial impact of listing mogamulizumab (Table 12).

Table 12: Key inputs for financial estimates

Data	Value applied and source	Comment
Market for relapsed/refractory MF/SS therapies without listing of mogamulizumab		
Estimated market (scripts) in 2024	435; Estimated as the number of scripts for vorinostat, brentuximab and methoxsalen during the most recent financial year (2023/2024) based on Medicare statistics.	This was appropriate. However, the estimated total number of scripts reported in the PBS statistics was lower than the total number of scripts in the FY 2023/2024 provided by the DUSC Secretariat (640).
Annual market growth	2.08% in year 1 to 1.78% in year 6; consistent with predicted growth in the Australian population aged 40 years or more.	The magnitude of market growth was reasonable.
Projected size of the current anti-CTCL market	81 in year 1 to 264 in year 6; Calculated 2023/24 scripts for vorinostat, brentuximab and methoxsalen and the assumed annual growth of anti-CTCL market.	This was appropriate.
Share of current market (status quo scenario without listing of mogamulizumab)	Vorinostat, 33% year 1 to 45% year 6; Brentuximab, 48% year 1 to 16% year 6; Methoxsalen, 19% year 1 to 39% year 6. Based on PBS utilisation data for 2023/24 of respective drugs in the absence of mogamulizumab.	The market share of vorinostat for 2023/24 was reasonable based on 2023/24 Medicare Statistics (31%, until June 2024). The market share of brentuximab was overestimated and that of methoxsalen was underestimated compared to Medicare Statistics for 2023/24 (35% for brentuximab and 35% for methoxsalen, until June 2024).
Market for relapsed/refractory MF/SS therapies with listing of mogamulizumab		
Uptake rate (rate of substitution) for vorinostat	Assumed from 20% in year 1 up to 80% in year 6.	The extent of substitution was uncertain and likely overestimated. Some patients may prefer treatment in the form of oral tablets.
Uptake rate (rate of substitution) for brentuximab	Assumed constant 25% across six years.	This was reasonable given the projected decline in its use.
Uptake rate (rate of substitution) for methoxsalen	Assumed from 10% in year 1 up to 60% by year 6.	This was reasonable given relatively stable projected market share.
Patient copayment	PBS: $28.19 RPBS: $3.11 Calculated as the mean of all PBS/RPBS services for vorinostat, brentuximab and methoxsalen sourced from PBS item statistics.	This was not appropriate as the resubmission applied the co-payment amounts from 2021. The impact of updating the co-payments was tested in a SA.
MBS costs	ECP: $2,108.25 MBS items 14247; 14249	This was appropriate. However, the resubmission did not include administration costs per infusion of mogamulizumab.

Source: Table 4-1 p178, Table 4-3 p179, Table 4-4 p180, Table 4-5 p180, Table 4-6 p181 of the resubmission, Section 4 Workbook
CTCL = Cutaneous T-Cell Lymphoma; ECP = extracorporeal photopheresis; FY = financial year; MBS = Medicare Benefits Schedule MF = mycosis fungoides; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; SA = sensitivity analysis; SS = Sezary syndrome

6.36 The resubmission projected the use and market share of existing treatments on the PBS/RPBS for CTCL i.e., vorinostat, brentuximab, methoxsalen and ECP in the absence of mogamulizumab. Subsequently, the resubmission estimated the substitution effect of listing mogamulizumab on the existing treatments to estimate the financial impact on Government health budgets over the 6-year forward estimates. The total number of scripts in FY 2023/2024 in the utilisation data provided by the DUSC Secretariat was

640, compared with the 435 scripts processed from July 2023-June 2024 as applied by the March 2025 resubmission in forming its financial estimates. This suggests that the number of scripts in the current market without mogamulizumab as presented by the resubmission was likely underestimated. The impact of applying the DUSC Secretariat data for 2023/2024 was tested in a sensitivity analysis and resulted in a higher financial expenditure over the 6 years compared with the base case results.

6.37 The resubmission assumed the market growth rate (2.12% to 1.85%) was consistent with predicted growth in the Australian population aged 40 years or more from which the vast majority of CTCL patients are diagnosed. This was reasonable.

6.38 The resubmission claimed that the majority of substitution would be from vorinostat for which there is the greatest overlap in the respective treated populations. The resubmission assumed that substitution would be gradual and incremental, mainly at the point of initiation of a new line of therapy. The substitution for vorinostat was 20% in year 1, increasing to 80% in year 6 of listing. The extent of substitution was uncertain and likely overestimated as some patients may prefer treatment with tablets (vorinostat), which may impact on the rate of substitution. The resubmission acknowledged that the substitution rate was uncertain.

6.39 The substitution of mogamulizumab for ECP and methoxsalen was assumed to be driven by clinician and patients' preferences. This was reasonable, but the extent of substitution was uncertain. The March 2025 resubmission assumed substitution for ECP and methoxsalen of 10% in year 1, increasing to 60% in year 6. However, the MSAC Evaluation Subcommittee noted that there was potential for ECP and methoxsalen to be used as combination therapy with other systemic treatments (p17, Application No. 1420.1 MSAC PSD, April 2020). The MSAC Evaluation Subcommittee also noted that ECP would only be available in major cities (p21, Application No. 1420.1 MSAC PSD, April 2020), which may imply that patients would prefer treatment with mogamulizumab.

6.40 The resubmission acknowledged the differences in dose relativities between mogamulizumab and all three comparators, weight-based dosing schedules (mogamulizumab and brentuximab), alternative recommended treatment regimens (ECP + methoxsalen) and differently timed loading phases (mogamulizumab and ECP + methoxsalen). To address these differences, the March 2025 resubmission assumed different script equivalence for the initial (3 month) and continuing phases of treatment. This was reasonable.

6.41 The estimated number of scripts dispensed, and financial implications of the proposed listing are summarised in Table 13.

6.42 The resubmission stated that the estimated number of items dispensed was consistent with a (point) prevalent treated population of approximately < 500 patients in year 1, increasing to < 500 by year 6. This was likely underestimated, particularly compared with the estimated number of patients presented in the July 2020

submission (< 500 in year 1 to < 500 in year 6) and November 2020 minor submission (< 500 in year 1 to < 500 in year 6).

Table 13: Estimated use and financial implications (using published price of brentuximab vedotin)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of mogamulizumab						
Cost to PBS/RPBS less copayments resubmission	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Cost to PBS/RPBS less copayments PSCR[a]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Estimated financial implications for vorinostat and brentuximab (published price), ECP + methoxsalen						
Cost to PBS/RPBS less copayments	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net financial implications						
Net cost to PBS/RPBS	[redacted][4]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to PBS/RPBS PSCR[a]	[redacted][4]	[redacted][4]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to MBS/ Services Australia/other	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net cost to PBS/RPBS/MBS/Services Australia	[redacted][4]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to PBS/RPBS/MBS/Services Australia in PSCR[a]	[redacted][4]	[redacted][4]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
July 2020 submission - estimated use and financial implications						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of scripts dispensed	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Net cost to PBS/RPBS	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
November 2020 resubmission - estimated use and financial implications						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of scripts dispensed	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Net cost to PBS/RPBS	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]

Source: Table 4-7 p181 of the resubmission, Table 4.9 p182 and Section 4 workbook (Sheet 4b), Table 4.9 p182 and Section 4 workbook (Sheet 4b), Table 4-11 p184 of the resubmission, Table 10, mogamulizumab Minutes, November 2020 PBAC Meeting

[a] Incorporates revised EMP of $[redacted] per vial offered in PSCR

ECP = extracorporeal photopheresis; MBS = Medical Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

Blue shading indicates data previously seen by the PBAC.

The redacted values correspond to the following ranges:

[1] *<500*

[2] *500 to <5,000*

[3] *$0 to <$10 million*

[4] *net cost saving*

6.43 Based on the revised effective price proposed in the PSCR, the net cost to the PBS/RPBS in year 6 of listing was estimated to be $0 to <$10 million, compared with $0 to <$10 million in the November 2020 resubmission. This difference was due to the

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lower price for mogamulizumab and changes in the assumptions about the substitution for current medicines.

6.44 The cost-saving to the PBS/RPBS in year 1 of listing was estimated to be net cost saving. However, the existence and extent of this reduction was uncertain, based on its use of the published price for brentuximab and its reliance on script numbers for the current market (2023/2024), which were lower than the total number of scripts for the same period provided by the DUSC Secretariat. The financial estimates over 6 years re-estimated using the data provided by the DUSC Secretariat were substantially higher than the base case. In addition, the magnitude of the mogamulizumab estimates was considered to be uncertain as the distribution of vorinostat community scripts between public and private scripts for mogamulizumab could not be verified.

6.45 The ESC noted that the resulting financial estimates were not cost neutral for this CMA and considered that this was likely due to mogamulizumab being estimated to impact the market share of not only vorinostat but also brentuximab and methoxsalen. The ESC noted that there were differences in dose relativities (see paragraph 6.40) resulting in mogamulizumab requiring a higher number of scripts compared to each of these agents. The CMA proposed in the PSCR was based on steady state dosing and hence did not account for the higher number of doses of mogamulizumab in the first cycle.

Financial Management – Risk Sharing Arrangements

6.46 No risk-sharing arrangement (RSA) was proposed. A RSA was not considered during the July 2020 and November 2020 PBAC Meetings.

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

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7 PBAC Outcome

7.1 The PBAC recommended the Authority Required listing of mogamulizumab for the treatment of patients with relapsed or refractory cutaneous T cell lymphoma (CTCL), on the basis that it should be available only under special arrangements under Section 100 (Efficient Funding of Chemotherapy Program). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of mogamulizumab would be acceptable if it were cost-minimised against vorinostat.

7.2 The PBAC welcomed the input from individuals who described the impact of relapsed or refractory CTCL on their quality of life, and from health care professionals who highlighted that durable remissions are not attained with one line of treatment. The PBAC noted the input from clinicians in the sponsor hearing regarding the limitations of treatment options currently available. The PBAC acknowledged that mogamulizumab has a unique mechanism of action and agreed with clinician advice that this agent would be particularly useful in patients with blood compartment involvement. The PBAC noted that all input, including that from the Leukaemia Foundation and Rare Cancers Australia, highlighted the need for new treatment options. Overall, the PBAC agreed with the input provided that there was a high clinical need for alternate therapy options for patients with this rare condition.

7.3 With regard to the requested listing and restriction, the PBAC advised that:

- An Authority Required (Written) listing was appropriate for the initial treatment phase and an Authority Required (Telephone) listing was appropriate for the continuing treatment phase.
- It was appropriate to align the clinical criteria of the restriction with that of the current vorinostat restriction as specified in paragraph 3.2.
- Specification of a maximum amount of 120 mg (without further administrative advice prohibiting requests for increased maximum quantities) was appropriate.
- Three repeats for the initial treatment restriction was appropriate as this would accommodate the weekly dosing on days 1, 8, 15 and 22 used for the first 28-day cycle. The PBAC considered that seven repeats was appropriate for the continuing treatment restriction where dosing would be administered every two weeks on days 1 and 15 of each subsequent 28-day cycle until disease progression or unacceptable toxicity.
- While a Special Pricing Arrangement (SPA) was requested, one does not apply to vorinostat which mogamulizumab is cost-minimised against. The PBAC noted that a decision on whether mogamulizumab would be eligible for a SPA would be a matter for the Government and not the PBAC.

7.4 The PBAC reaffirmed its previously expressed view that the proposed comparator of vorinostat was appropriate (paragraph 7.3, mogamulizumab PSD, July 2020 PBAC Meeting). The PBAC noted that no formal claim was made in relation to the secondary

comparator extracorporeal photopheresis or the tertiary comparator brentuximab vedotin in the resubmission.

7.5 The PBAC noted the key clinical evidence provided in the resubmission was based on the MAVORIC trial (N=372), which compared mogamulizumab and vorinostat, and the ANCLD (Australian National Cutaneous Lymphoma Database) study for vorinostat (N=64). The PBAC recalled that it had previously considered that the extent of benefit for mogamulizumab versus vorinostat could not be determined from the MAVORIC trial given the high and early level of crossover of vorinostat patients to mogamulizumab (paragraphs 7.4, 7.5, and 7.7, mogamulizumab PSD, July 2020 PBAC Meeting).

7.6 The PBAC noted that the resubmission had presented an unanchored matching-adjusted indirect comparison (MAIC) for the outcome of overall survival (OS) by matching individual patient data (based on sex and CTCL subtypes) from patients treated with mogamulizumab in MAVORIC to summary-level patient data for vorinostat in ANCLD. The PBAC noted that the results of the MAIC did not reach the 0.05 nominal level of significance (hazard ratio = 0.68; 95% confidence interval = 0.45, 1.02; p = 0.06). The PBAC noted that the limited amount of data available for patients in the ANCLD study impacted the robustness of the MAIC, and overall, the PBAC considered that the MAIC was unreliable for decision making. The PBAC considered the claim of superior clinical effectiveness versus vorinostat was not supported by the data presented. However, the PBAC considered a claim of non-inferior comparative effectiveness was reasonable.

7.7 The PBAC noted that no new safety data were available and reaffirmed its July 2020 advice that the claim of non-inferior comparative safety versus vorinostat was reasonable (paragraph 7.8, mogamulizumab PBAC PSD, July 2020 PBAC Meeting).

7.8 The PBAC noted that the resubmission had presented a cost-utility analysis based on the clinical claim of superiority, which it considered was not supported by the data presented (see paragraph 7.7). The PBAC noted that the PSCR presented a cost-minimisation approach (CMA) of mogamulizumab versus vorinostat. The PBAC considered dosing based on steady-state was reasonable but noted the CMA did not include the cost of mogamulizumab administration or adjust for dose intensity, which it considered was inappropriate. The PBAC agreed with the ESC that, although uncertain, it would be reasonable to assume the treatment duration of mogamulizumab and vorinostat would be the same in clinical practice. As such, the PBAC considered the CMA outlined in Table 9 which assumed equal treatment duration, dosing based on steady-state, adjusting for mean dose intensity of mogamulizumab and vorinostat in MAVORIC and including the cost of administration of mogamulizumab was appropriate. The PBAC advised that the following equi-effective dosing over a 28-day cycle were appropriate for the CMA:

- 400 mg vorinostat administered orally daily, adjusted for dose intensity (88.96%)

- 80 mg of mogamulizumab administered IV on days 1 and 15 only, adjusted for dose intensity (94.41%).

7.9 The PBAC noted that data from the DUSC Secretariat suggested that the resubmission had underestimated the market size and that the financial expenditure over 6 years may be higher than estimated. The PBAC accepted the resubmission market share inputs and the rates of substitution proposed for vorinostat, brentuximab vedotin and methoxsalen. However, the PBAC advised that the financial estimates should be revised to incorporate the PBS statistics provided by the DUSC Secretariat, the effective price of brentuximab vedotin and the outcome of the CMA outlined in paragraph 7.8. The PBAC agreed with the ESC that it was likely that the resulting financial estimates would not be cost neutral for this CMA as mogamulizumab was being estimated to impact the market share of not only vorinostat but also brentuximab vedotin and methoxsalen (see paragraph 6.45). The PBAC considered the additional cost was reasonable as mogamulizumab would be used as another treatment option to those currently available in this rare disease and would be valuable to enable patients to access therapies in centres closer to home (as compared to extracorporeal photopheresis) and for different disease scenarios or manifestations.

7.10 The PBAC advised that mogamulizumab should not be treated as interchangeable with any other drugs.

7.11 The PBAC advised that mogamulizumab is not suitable for prescribing by nurse practitioners.

7.12 The PBAC recommended that the Early Supply Rule should not apply.

7.13 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because mogamulizumab is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over vorinostat, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

7.14 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

MEDICINAL PRODUCT Form	PBS item code	Max. Amount	№.of Rpts
MOGAMULIZUMAB Injection	NEW (Public) NEW (Private)	120 mg	3
Available brands			
Poteligeo mogamulizumab 20 mg/5 mL injection, 5 mL vial			
Restriction Summary [new1] / Treatment of Concept: [new1A]			
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
	Prescriber type: ☒Medical Practitioners		
	Restriction type: ☒Authority Required (FULL assessment) in writing only via post/HPOS upload)		
Prescribing rule level	**Administrative Advice:** No increase in the maximum number of repeats may be authorised.		
	Condition: Cutaneous T-cell lymphoma		
	Indication: Cutaneous T-cell lymphoma		
	Treatment Phase: Initial treatment		
	Clinical criteria:		
	Patient must have received systemic treatment with chemotherapy		
	AND		
	Clinical criteria		
	Patient must demonstrate relapsed or chemotherapy-refractory disease		
	AND		
	Clinical criteria		
	Patient must be ineligible for stem cell transplant		
	AND		
	Clinical criteria:		
	The treatment must be the sole PBS-subsidised therapy for this condition		
	Prescribing Instructions: Applications for authorisation of initial treatment must be in writing and must include: (a) details of the proposed prescription; and (b) a completed cutaneous T-cell lymphoma (CTCL) initial PBS Authority Application - Supporting Information Form		
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authorisation under this restriction should be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/hpos) Alternatively, applications for authority to prescribe can be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826		

	HOBART TAS 7001

MEDICINAL PRODUCT **Form**	**PBS item code**	**Max. Amount**	**№.of Rpts**
MOGAMULIZUMAB (mogamulizumab 20 mg/5 mL injection, 5 mL vial) Injection	NEW (Public) NEW (Private)	120 mg	7
Available brands			
Poteligeo (mogamulizumab 20 mg/5 mL injection, 5 mL vial)			
Restriction Summary [new2] / Treatment of Concept: [new2A]			
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
	Prescriber type: ☒Medical Practitioners		
	Restriction type: ☒Authority Required - Immediate assessment (telephone / online)		
Prescribi 7607	**Administrative Advice:** No increase in the maximum number of repeats may be authorised.		
	Condition: Cutaneous T-cell lymphoma		
	Indication: Cutaneous T-cell lymphoma		
	Treatment Phase: Continuing treatment		
	Clinical criteria:		
	Patient must have previously received PBS-subsidised treatment with this drug for this condition		
	AND		
	Clinical criteria:		
	Patient must not have progressive disease while receiving PBS-subsidised treatment with this drug for this condition		
	AND		
	Clinical criteria:		
	The treatment must be the sole PBS-subsidised therapy for this condition		
	Prescribing Instructions: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m.Monday to Friday).		

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

9 Context for Decision

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

OFFICIAL

10 Sponsor's Comment

The sponsor had no comment.

OFFICIAL

Addendum to the March 2025 PBAC Minutes:

3.01 MOGAMULIZUMAB, Solution concentrate for I.V. infusion 20 mg in 5 mL, Poteligeo®, Kyowa Kirin Australia Pty Ltd.

11 Sponsor proposal

11.1 Following the March 2025 PBAC meeting, the sponsor wrote to the Department and proposed 'as a best and final offer', an effective ex-manufacturer price of $[redacted]. This was a higher price than would result from the PBAC-recommended CMA in March 2025 (in paragraph 7.8 and Table 9).

11.2 The sponsor outlined that it was unable to progress with listing on the basis recommended by PBAC and highlighted:

"CTCL is a rare, aggressive, and incurable type of cancer, with which around 40 Australians are diagnosed each year, that causes intense suffering and major life disruption. In consideration of extensive input from clinicians and affected individuals, the PBAC agreed that there is a high clinical need for alternate therapy options for patients with this rare condition.

Mogamulizumab represents an attractive new treatment option for CTCL, which the PBAC has acknowledged has a unique mechanism of action and would be particularly useful in patients with blood compartment involvement. Since its approval by the FDA in 2018, mogamulizumab has become an internationally established standard of care, which is widely considered by clinical experts to be superior to other available therapies, for at least this subgroup of patients."

11.3 The PBAC noted that applying the current MBS Item 13950 85% benefit ($107.10, from 1 July 2025), and 100% dose intensity to both medicines in the CMA in results in an AEMP of $[redacted].

11.4 The PBAC noted that the sponsor's offer of $[redacted] represents a [redacted]% premium over a CMA price of $[redacted] (i.e. derived from applying the 1 July 2025 85% MBS Benefit and the mean dose intensities from the MAIVORIC trial).

12 PBAC Outcome

12.1 The PBAC recalled its previous advice regarding the high clinical need for alternative therapy options for this rare disease, and its advice that mogamulizumab has a unique mechanism of action which would be particularly useful in patients with blood compartment involvement. The PBAC considered that a small premium over the

previously recommended CMA was appropriate to reflect the additional benefits that these patients would receive with treatment with mogamulizumab.

12.2 Therefore, the PBAC advised that mogamulizumab would be acceptably cost-effective at the price in the sponsor's post-PBAC proposal.

Outcome:
Advice Provided

13 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.

14 Sponsor's Comment

The sponsor had no comment.