Record of the Cancer Treatments Advisory Committee Meeting held on 9 October 2025

Cancer Treatments Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Cancer Treatments Advisory Committee meeting; only the relevant portions of the meeting record relating to Cancer Treatments Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Cancer Treatments Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Stephen Munn - Chair
Allanah Kilfoyle
Chris Frampton
Lochie Teague
Matthew Strother
Vidya Mathavan

Apologies
Alice Minhinnick
Michelle Wilson
Oliver Brake
Richard Isaacs
Scott Babington

2. Summary of recommendations

	Pharmaceutical and Indication	Recommendation
7.3	Polatuzumab vedotin for people with diffuse large B-cell lymphoma (International Prognostic Index = 2-5), subject to Special Authority criteria	Low Priority
7.4	Polatuzumab vedotin for people with diffuse large B-cell lymphoma (International Prognostic Index = 3-5), subject to Special Authority criteria	Medium Priority
8.3	Glofitamab (with gemcitabine and oxaliplatin) be funded for people with relapsed or refractory diffuse large B-cell lymphoma in the ≥ second line setting, subject to Special Authority criteria	High Priority
8.4	Epcoritamab be funded for people with relapsed or refractory diffuse large B-cell lymphoma in the ≥3rd line setting, subject to Special Authority criteria	High Priority
9.3	Momelotinib for the first-line treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF, with moderate to severe anaemia, subject to Special Authority criteria	Cost neutral – to ruxolitinib
9.6	Momelotinib for the second-line treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF, with	High Priority

	moderate to severe anaemia, subject to Special Authority criteria	

These recommendations were made within the context of treatments of malignancy.

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Cancer Treatments Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 6.4 of the SAC Terms of Reference.

3.3. The Cancer Treatments Advisory Committee is a Specialist Advisory Committee of Pharmac. The Cancer Treatments Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Cancer Treatments Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Cancer that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Cancer that differ from the Cancer Treatments Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

3.4. Pharmac considers the recommendations provided by both the Cancer Treatments Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Cancer.

4. Welcome and introduction

4.1. The Chair welcomed the committee with a karakia followed by whakawhanaungatanga.

5. Pharmac Update

5.1. The Committee noted the Pharmac Update.

5.2. The Committee acknowledged the recent changes in Pharmac kaimahi and ongoing leadership and strategic changes, including the new Chief Executive who started at Pharmac in mid-September and the recent release of the 2025/2026 Letter of Expectations.

5.3. The Committee noted an update about the organisation reset programme and acknowledged that more information can be found on the Pharmac Website.

5.4. The Committee noted the following updates to the record processes:

5.4.1. 30-day provisional recommendation trial update.

5.4.2. The Committee noted the removal of second committee reviews, with targeted reviews to be used as required, and supported the use of direct engagement with Discussion Leads to resolve outstanding issues.

6. Matters Arising

[redacted]

Withheld – 9 (2)(b)(ii) OIA

[redacted]

7. Polatuzumab vedotin for the first-line treatment of diffuse large B-cell lymphoma

Application

7.1. The Committee reviewed the application for polatuzumab vedotin (with rituximab, cyclophosphamide, doxorubicin, and prednisone) for the first-line treatment of diffuse large B-cell lymphoma.

7.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

7.3. The Committee **recommended** that polatuzumab vedotin be funded with a **low priority** for people with diffuse large B-cell lymphoma (International Prognostic Index = 2-5), within the context of treatments of malignancy and subject to the following Special Authority criteria:

> Initial application – diffuse large B-cell lymphoma
> Applications from any relevant practitioner. Approvals valid for 6 months.
> All of the following:
> 1. Patient has a diagnosis of diffuse large B-cell lymphoma (DLBCL) by biopsy; AND

2. Patient has not previously received any treatment for DLBCL; AND
3. Patient has an International Prognostic Index (IPI) score of 2-5; and
4. Treatment with polatuzumab vedotin is for a maximum period of 6 cycles; and
5. Treatment with polatuzumab vedotin is to be received in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone

7.4. The Committee **recommended** that polatuzumab vedotin be funded with a **medium priority** for people with diffuse large B-cell lymphoma (International Prognostic Index = 3-5), within the context of treatments of malignancy and subject to the following Special Authority criteria:

Initial application – diffuse large B-cell lymphoma
Applications from any relevant practitioner. Approvals valid for 6 months.
All of the following:

1. Patient has a diagnosis of diffuse large B-cell lymphoma (DLBCL) by biopsy; AND
2. Patient has not previously received any treatment for DLBCL; AND
3. Patient has an International Prognostic Index (IPI) score of 3-5; and
4. Treatment with polatuzumab vedotin is for a maximum period of 6 cycles; and
5. Treatment with polatuzumab vedotin is to be received in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone

7.5. In making these recommendations, the Committee considered:

7.5.1. Many people with diffuse large B-cell lymphoma relapse or are refractory to the available 1st line treatment (R-CHOP), which creates a high health need for more effective first-line options.

7.5.2. More efficacious 1st line treatments would spare a larger proportion of individuals from progressing to the relapsed or refractory disease setting where treatment options have low efficacy and significant toxicity.

7.5.3. The available evidence suggests polatuzumab vedotin (with R-CHP) offers a modest gain in progression free survival that would be meaningful for individuals and their whānau.

7.5.4. That the health benefit appeared more pronounced in patients with IPI scores of 3–5 compared with those with an IPI score of 2.

Discussion

Māori impact

7.6. The Committee discussed the impact of funding polatuzumab vedotin on Māori Health outcomes and noted that diffuse large B-cell lymphoma (DLBCL) was not one of the 5 stated Māori health areas of focus | Hauora Arotahi. Members noted that mortality rates for non-Hodgkin's lymphoma are higher for Māori than for people of European descent (Clough et al. Cancer Epidemiol. 2024;93:102656), but were not aware of data specific to DLBCL.

Populations with high health needs

7.7. The Committee discussed the health need(s) associated with DLBCL among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other groups identified to have high health needs by the Government Policy Statement on Health 2024-2027. The Committee considered they were not aware of evidence indicating these groups were overrepresented in this therapeutic setting. The Committee considered they were not aware of reasons why these groups would not benefit similarly if polatuzumab vedotin were funded compared to populations not identified to have high health needs but acknowledged that systemic inequalities can negatively impact timely diagnosis and treatment.

Background

7.8. The Committee noted that this was its first consideration of an application for polatuzumab vedotin.

7.9. The Committee noted that polatuzumab vedotin (with R-CHP; rituximab, cyclophosphamide, doxorubicin, and prednisone) was being reviewed for its use as a 1st line treatment for people with DLBCL, with an international prognostic index score (IPI) ≥ 2. The Committee noted the submission included evidence for a higher risk sub-population restricted to IPI ≥ 3.

Health need

7.10. The Committee noted DLBCL not otherwise specified is fatal if not cured and accounts for >80% of all large B-cell lymphomas (Sehn & Salles, NEJM. 2021;384:842-58). Members noted the prognosis of this heterogenous disease can be stratified by an individual's number of IPI risk factors. When treated with chemoimmunotherapy, approximate 4-year overall survival (OS) for IPI 0 = 94%, IPI 1-2 = 79%, IPI 3-5 = 55% (Sehn et al. Blood. 2007;109:1857-61).

7.11. The Committee noted the standard of care in New Zealand was a chemoimmunotherapy regimen of 6 cycles of rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP).

7.12. The Committee noted that approximately 30-40% of patients will relapse or be refractory to R-CHOP in the 1st-line setting (Sehn & Salles, NEJM. 2021). Members noted individuals who progress following treatment in the 1st line setting are faced with a poor prognosis, and the available salvage treatment options (e.g. high-dose chemotherapy followed by autologous stem cell transplant (ASCT)) are associated with low efficacy, significant toxicity, and notable detriments to quality of life. The Committee noted that not all individuals are eligible for ASCT, and for those who are, the intensive procedure is associated with a 1–3% mortality rate (Berro et al. Biol Blood Marrow Transplant. 2020;26:1828-32), requires 2–3 weeks of inpatient care, and involves a physical recovery period of approximately 6 weeks.

7.13. The Committee considered there was an unmet health need for more efficacious first line therapies that would spare people from progressing into the relapsed or refractory DLBCL disease state.

7.14. The Committee noted Ministry of Health Cancer Registrations data that estimated that 373 new cases of DLBCL are reported annually in New Zealand and considered the estimate to be reasonable.

Health benefit

7.15. Polatuzumab vedotin is an antibody drug conjugate that specifically targets CD79b with a payload of the microtubule-disrupting agent monomethylauristatin E.

7.16. The Committee noted that the proposed regimen would replace vincristine in R-CHOP with polatuzmab vedotin (pola-R-CHP).

7.17. The Committee noted the POLARIX randomised controlled trial as key evidence (Tilly et al. NEJM. 2021;386:351-63). POLARIX was an international, phase III, double-blind, placebo-controlled study that randomly assigned treatment naïve individuals with DLBCL (IPI = 2-5) to receive either six cycles of pola-R-CHP (polatuzumab vedotin replacing vincristine in R-CHOP; n=440) or 6 cycles of standard R-CHOP (n=439), followed by two cycles of rituximab monotherapy (both arms).

7.17.1. The Committee discussed the toxicity of pola-R-CHP compared to R-CHOP, and considered the evidence indicated an increased risk of febrile neutropenia for those receiving pola-R-CHP (14.3%) compared to those on R-CHOP (8.0%). The Committee noted the similar incidence between study arms of any-grade adverse events, serious adverse events, and adverse events

leading to treatment discontinuation, and considered that switching vincristine for polatuzumab vedotin did not materially increase the regimen's toxicity.

7.17.2. The Committee noted the findings from the 5-year follow-up intention-to-treat analysis (Morschauser et al. J Clin Oncol. 2025;JCO2500925), and considered there to be an advantage in 5-year PFS for those receiving pola-R-CHP (64.9%, 95%CI: 58.8-70.0) compared to R-CHOP (59.1%, 95%CI: 54-64.3), with a hazard ratio of 0.77 (95%CI: 0.62-0.97). The Committee considered 5-year OS and considered the treatment effect appeared similar for pola-R-CHP (82.3%, 95%CI: 78.7-85.9) and R-CHOP (79.5%, 95%CI: 75.7-85.9) with a 5-year OS hazard ratio of (0.85, 95%CI: 0.63-1.15). The Committee discussed the maturity of the OS data at 5 years, and considered that a significant difference in OS may still emerge with a longer duration of follow-up. Overall, the Committee considered the treatment with pola-R-CHP to offer a modest but meaningful health gain compared to R-CHOP.

7.17.3. The Committee noted that a lower proportion of patients who received pola-R-CHP (25.5%) required subsequent anti-lymphoma therapies compared to those who received R-CHOP (35.3%).

7.17.4. The Committee discussed efficacy outcomes stratified by IPI, and noted 38% of study participants were IPI = 2, while 62% were IPI = 3-5. The Committee noted there was a 5-year PFS advantage favouring pola-R-CHP for participants who were IPI = 3-5 (HR: 0.72, 95%CI: 0.56-0.94), but no statistically significant difference between study arms was observed from the IPI = 2 subgroup (HR: 0.91, 95%CI: 0.61-1.36). The Committee noted there was no statistically significant difference in 5-year OS for participants on pola-R-CHP reported for either the IPI = 2 subgroup (HR: 0.96, 95%CI: 0.53-1.75) or the IPI = 3-5 subgroup (HR: 0.81, 95%CI: 0.57-1.15). However, the Committee considered the IPI = 3–5 subgroup appeared to potentially capture an emerging difference in favour of pola-R-CHP. The Committee considered that pola-R-CHP did not appear to offer any additional benefit compared to R-CHOP for individuals in the IPI = 2 subgroup but noted that POLARIX was not powered to detect significant differences by IPI subtype.

7.17.5. The Committee discussed the reported efficacy stratified by cell of origin, as determined by NanoString (NGS-detected). The Committee considered there was evidence in favour of pola-R-CHP in the activated B-cell (ABC) subtype, but no statistically significant benefit in the germinal centre B-cell (GCB) subtype. The committee noted that the POLARIX was not powered to detect significant differences by cell of origin.

7.17.6. The Committee considered POLARIX to be a well conducted randomised controlled trial of reasonable size and considered the quality of evidence to be good. The Committee considered that most haematologists in New Zealand do not administer the additional 2 cycles (Cycle 7 & 8) of rituximab given to both study arms in POLARIX. The Committee considered the results were generalisable to the New Zealand population.

7.18. The Committee discussed ongoing investigations of polatuzumab vedotin in the relapsed setting and noted the findings of the Phase 1b/2 GO29365 extension study (Sehn et al. Blood Adv 2022;6:533-43), which reported that participants with relapsed DLBCL who received polatuzumab vedotin with bendamustine and rituximab had a more favourable median PFS and OS compared with those who received bendamustine with rituximab alone. The Committee acknowledged interest in the clinical community in using polatuzumab vedotin as a bridge to CAR-T therapy in the relapsed setting.

Suitability

7.19. The Committee noted that funding polatuzumab vedotin would be expected to have a minimal impact on the system resources required to provide treatment relative to R-CHOP. Vincristine infusion (~15 min) would be replaced by polatuzumab vedotin (90 min infusion in cycle 1, 30 min infusions thereafter). The Committee considered that infusing polatuzumab vedotin carries a manageable risk of infusion reactions, comparable to those associated with rituximab, and would be appropriate for administration in outpatient settings without materially changing clinic resourcing or training.

Cost & Savings

7.20. The Committee noted the submission included in estimation that 256 New Zealanders would be eligible for treatment in 2026, and considered this estimation was likely to be low.

7.21. The Committee considered that the estimated uptake of 60% in the first year appeared low and noted that it was likely most New Zealand haematologists would switch from R-CHOP to pola-R-CHP immediately.

7.22. The Committee considered the cure rates included in the submission for ASCT for people who relapse early (18%) and who are in the late relapse health state (53%) and considered these estimates to be reasonable.

7.23. The Committee considered that the supplier's assumption whereby patients remaining in the progression free state after a defined period of time are transitioned to the "cured" health state, was reasonable.

7.23.1. The Committee noted the findings of Maurer et al. J Clin Oncol 2014;32:1066-73, which reported people with DLBCL who reach event-free status 24 months from diagnosis have an overall survival equivalent to that of the age- and sex-matched general population, and considered those who reach two years without progression are highly likely to be cured.

7.23.2. The Committee noted that the timepoint for considering patients cured was uncertain.

7.24. The Committee considered there would likely be savings to the health system from having a higher cure rate in the 1st line setting.

7.25. The Committee noted the increased rate of febrile neutropenia with Pola-R-CHP compared to R-CHOP and considered that most individuals presenting with febrile neutropenia would require inpatient admission for at least 72 hours.

7.26. The Committee considered the two additional cycles (cycle 7 & 8) of rituximab monotherapy are not provided routinely in New Zealand practice for R-CHOP and would likely not be administered with pola-R-CHP if polatuzmab vedotin were to be funded.

Funding criteria

7.27. The Committee discussed the option of restricting access to polatuzumab by cell-of-origin (ABC vs GCB) but considered that NanoString-based assignment is not widely available in New Zealand, and Hans immunohistochemistry would not provide an equivalent analytical method.

7.28. The Committee considered making separate funding recommendations for the IPI = 3–5 and IPI = 2–5 subgroups to be appropriate but acknowledge that this is based on an underpowered subgroup analysis.

7.29. The Committee considered that a criterion restricting access by performance status (ECOG 0–2) was not required to sufficiently target the intended population, despite being an eligibility criterion for POLARIX.

Summary for assessment

7.30. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for polatuzumab vedotin if it were to be funded in New Zealand for diffuse large B-cell lymphoma. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Adults with previously untreated diffuse large B-cell lymphoma (DLBCL), and an international prognostic index (IPI) of 2-5 Separate consideration of the subgroup with IPI 3-5
Intervention	Polatuzumab vedotin 1.8 mg/kg, cyclophosphamide 750 mg/m2, doxorubicin 50 mg/m2, rituximab 375 mg/m2 BSA, administered intravenously on day 1 of each treatment cycle and prednisone 100 mg administered orally on days 1 to 5 of the treatment cycle (Pola+R-CHP). Treatment for six cycles. Cycles 7 and 8 consist of rituximab as monotherapy*. *However, based on input from haematologists, it is understood there is variable use of rituximab monotherapy in Cycles 7 and 8 for the standard of care R-CHOP treatment course, so there is uncertainty whether this would be utilised in the Polatuzumab vedotin treatment course.
Comparator(s)	Cyclophosphamide 750 mg/m2, doxorubicin 50 mg/m2, vincristine 1.4 mg/m2, rituximab 375 mg/m2 BSA, administered intravenously on day 1 of the treatment cycle and prednisone 100 mg administered orally on days 1 to 5 of each treatment cycle (R-CHOP). Treatment for six cycles. Two additional cycles of rituximab monotherapy may be administered if considered necessary by the treating physician. However, insights from New Zealand haematologists suggest that these two cycles of rituximab are rarely administered
Outcome(s)	PFS • **IPI 2-5:** POLARIX reported an estimated 5-year PFS of 64.9% (95%CI: 58.8-70.0) for Pola+R-CHP and 59.1% (95%CI: 54.0-64.3) for R-CHOP with a HR of 0.77 (0.62-0.97) • **IPI 3-5:** POLARIX reported an estimated 5-year PFS of 63.2% for Pola+R-CHP and 53.5% for R-CHOP with a HR of 0.72 (95%CI: 0.55-0.94) OS • **IPI 2-5:** POLARIX reported an estimated 5-year OS of 82.3% (95%CI: 78.7-85.9) for Pola+R-CHP and 79.5% (95%CI: 75.7-83.4) for R-CHOP with a HR of 0.85 (95%CI: 0.63-1.16) • **IPI 3-5:** POLARIX reported an estimated 5-year OS of 79.2% for Pola+R-CHP and 74.7% for R-CHOP with a HR of 0.81 (95%CI: 0.57-1.15)
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	

8. Bispecific antibodies (glofitamab and epcoritamab) for relapsed or refractory diffuse large B-cell lymphoma

Application

8.1. The Committee reviewed two applications regarding bispecific antibodies for the treatment of relapsed or refractory diffuse large B-cell lymphoma:

8.1.1. Glofitamab with chemotherapy (gemcitabine and oxaliplatin) for people who have relapsed or been refractory to at least one prior treatment (≥2rd line)

8.1.2. Epcoritamab for people who have relapsed or been refractory to at least two prior treatments (≥3rd line)

8.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

8.3. The Committee **recommended** that glofitamab (with gemcitabine and oxaliplatin) be funded for people with relapsed or refractory diffuse large B-cell lymphoma in the ≥2rd line setting with a **high priority** within the context of the treatment of malignancy, subject to the following Special Authority criteria:

> **GLOFITAMAB with gemcitabine and oxaliplatin**
> **Initial application — relapsed or refractory diffuse large B-cell lymphoma**
> Applications from any relevant practitioner. Approvals valid for 9 months meeting the following criterial:
> All of the following:
> 1. Individual has been diagnosed with diffuse large B-cell lymphoma
> 2. Treatment is provided in combination with gemcitabine and oxaliplatin
> 3. Either:
> 3.1. The condition must have relapsed, or be refractory to, at least one prior treatment and the patient is ineligible for autologous stem cell transplant, **OR**
> 3.2. Patient has relapsed on two or more lines of therapy

8.4. The Committee **recommended** that epcoritamab be funded for people with relapsed or refractory diffuse large B-cell lymphoma in the ≥3rd line setting with a **high priority** within the context of the treatment of malignancy, subject to the following Special Authority criteria:

> **EPCORITAMAB**
> **Initial application — relapsed or refractory diffuse large B-cell lymphoma**
> Applications from any relevant practitioner. Approvals valid for 9 months meeting the following criterial:
> All of the following:
> 1. Individual has been diagnosed with diffuse large B-cell lymphoma
> 2. The condition must have relapsed following, or be refractory to, at least two prior systemic therapies, including at least one anti-CD20 monoclonal antibody-containing therapy.
> 3. Epcoritamab will be used as monotherapy
>
> **Renewal Application — relapsed or refractory diffuse large B-cell lymphoma**
> Applications only from a relevant specialist or any other medical practitioner on the recommendation of a relevant specialist. Approvals valid for 9 months where treatment remains clinically appropriate, and the patient is benefitting from treatment.

8.5. In making these recommendations the Committee considered:

8.5.1. The high and unmet health need associated with the lack of efficacious treatments for people with relapsed or refractory diffuse large B-cell lymphoma.

8.5.2. The treatment effect from either glofitamab (with chemotherapy) or epcoritamab represents a major health gain over the currently available salvage chemotherapy regimens, and that funding either medicine would provide a

chance of long-term remission (cure) in a proportion of people who would otherwise face an unfavourable disease prognosis and poor outcomes.

8.5.3. Glofitamab and epcoritamab are associated with cytokine release syndrome but are generally well-tolerated and have manageable risk profiles in the context of treatment.

Discussion

Māori impact

8.6. The Committee discussed the impact of funding glofitamab and/or epcoritamab on Māori Health outcomes and noted that diffuse large B-cell lymphoma (DLBCL) was not one of the 5 stated Māori health areas of focus | Hauora Arotahi. The Committee agreed with the Māori impact considerations outlined in the Polatuzumab vedotin record item and noted they had no additional comments.

Populations with high health needs

8.7. The Committee discussed the health need(s) associated with relapsed or refractory DLBCL (RR-DLBCL) among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other groups identified to have high health needs by the Government Policy Statement on Health 2024-2027. Members considered they were not aware of any reasons why people from these groups would benefit less from glofitamab or epcoritamab, if funded, compared with populations not identified as having high health needs. The Committee also considered they were not aware these groups were overrepresented in this therapeutic setting.

Background

8.8. The Committee noted that glofitamab with gemcitabine and oxaliplatin (GemOx) was being considered in the ≥2nd line RR-DLBCL setting, while epcoritamab was being considered in the ≥3rd line setting.

8.9. The Committee noted the glofitamab submission also included evidence for glofitamab (monotherapy) in the ≥3rd line RR-DLBCL setting, however, this was not the focus of the submission and a separate application would likely be required to support a fulsome review.

Health need

8.10. The Committee discussed the treatment paradigm for DLBCL and noted that while treatment in the 1st line setting is delivered with curative intent, approximately 10-15% of people are refractory to the standard of care, and an additional 20-25% of people relapse following treatment (Sehn et al. N Engl J Med. 2021;384:842-58). Members noted that overall, 30-40% of people with DLBCL progress to the relapsed or refractory disease setting.

8.11. The Committee considered those who progress to RR-DLBCL face a poor prognosis with a limited life expectancy given the currently available treatments. Members considered this aggressive disease to be associated with a substantial detriment to quality-of-life, including severe physical symptoms (e.g. fatigue and pain) and pronounced psychological distress for those affected and their whānau, particularly as progression to RR-DLBCL marks a shift from receiving treatment with curative intent to a disease state with substantially reduced likelihood of long-term survival.

8.12. The Committee considered that treatment for people with RR-DLBCL in New Zealand commonly begins with a salvage chemotherapy regimen (e.g. Rituximab combined with ifosfamide, carboplatin and etoposide (R-ICE), rituximab combined with gemcitabine and oxaliplatin (R-GemOx), or rituximab combined with gemcitabine, dexamethasone and cisplatin (R-GDP)). Members considered the available evidence indicates that no one salvage regimen has been shown to be superior to another. The

Committee noted that for those with chemotherapy-sensitive RR-DLBCL, following with autologous stem-cell transplantation (ASCT) offers the best chance of cure, however, only half of the individuals with RR-DLBCL are estimated to be both responsive to chemotherapy and considered eligible for ASCT (Sehn et al. 2021). Members considered that for individuals who are ineligible for ASCT, the available salvage regimens provide limited clinical benefit and are associated with considerable toxicity.

8.13. The Committee considered that once individuals relapse or become refractory to two or more systemic therapies, the ≥3rd line treatment landscape is highly variable in New Zealand. The Committee noted the epcoritamab submission identified R-GDP as the comparator in this setting and considered this to be reasonable. However, members considered that for people in this group, the limited clinical benefit of a third line of chemotherapy must be weighed against the associated toxicity and detriment to quality of life, and many individuals in this group would receive care with palliative intent and would not receive a third line of chemotherapy.

8.14. The Committee considered there to be a large and unmet health need for effective treatment options for people with RR-DLBCL, particularly for people who are not eligible for ASCT.

Health benefit

8.15. The Committee noted that both glofitamab and epcoritamab are bispecific antibody T-cell engagers (BiTE).

8.16. The Committee noted STARGLO as key evidence (Abramson et al. Lancet. 2024;404: 1940-54). STARGLO was an international, phase III, randomised (2:1), open-label study conducted at 62 centres across 13 countries in Asia, Australia, Europe, and North America. It investigated Glofit-GemOx (glofitamab plus GemOx; n=183) versus R-GemOx (rituximab plus GemOx; n=91) in ASCT-ineligible patients with histologically confirmed RR-DLBCL in the ≥2nd line setting. The primary endpoint was overall survival (OS). Members noted that of the 274 participants enrolled, 58% were male, and the median age was 68 years. In the updated analysis, the median follow-up duration was 20.7 months, however, the Committee also reviewed unpublished findings from the two- and three-year follow-up datasets.

8.16.1. The Committee noted that compared to R-GemOx, Glofit-GemOx was associated with a significant advantage in OS, progression free survival (PFS), and complete response rate (CR). The Committee noted from the updated analysis (median follow up: 20.7 months), that median OS [95% CI] from the Glofit-GemOx arm was 25.5 months [18.3-not estimable] compared to 12.9 months [7.9-18.5] with R-GemOx (HR:0.62, p:0.0064). The Committee considered the findings from the updated analysis to be further supported by the findings from the matured two- and three-year datasets. Overall, the committee considered the available evidence indicated a clear survival advantage in favour of Glofit-GemOx.

8.16.2. The Committee noted the additional toxicity associated with Glofit-GemOx compared to R-GemOx. As reported in the updated analysis, 54% of those receiving glofitamab (with GemOx) experienced a serious adverse event, compared to 17% of those receiving R-GemOx. Members further noted that 44% of people receiving glofitamab experienced cytokine release syndrome (CRS) which was predominately grade 1-2. Overall, members considered the risk profile of Glofit-GemOx to be generally manageable and regarded the additional risk as acceptable within the context of treatment.

8.16.3. The Committee discussed the quality of STARGLO, and noted while the study was open-label, they considered the overall trail design and resulting evidence to be of high quality. The Committee noted that efficacy outcomes were scored

by an independent review committee (IRC). The Committee noted that 37% of patients had received two prior lines of therapy, while 63% had received 1 prior line of treatment. The Committee noted that 7-8% of participants received prior car-T cell therapy, which is not currently funded in NZ. Overall, the Committee considered the evidence to be generalisable to the New Zealand context.

8.17. The Committee noted EPCORE NHL-1 as key evidence for the use of epcoritamab in the ≥3rd line RR-DLBCL setting. EPCORE NHL-1 was an international, multicentre, phase I/II, open-label trial that investigated epcoritamab in adults with RR-DLBCL. Eligible participants had an ECOG performance status of 0–2, had received insufficient benefit from at least two prior systemic therapies (including one anti-CD20 monoclonal antibody), and were either ineligible for or had failed ASCT. The pivotal cohort included 139 participants who received epcoritamab monotherapy. The primary endpoint was IRC-assessed overall response rate (ORR). Members noted that the median age was 68 years and the median follow-up duration at the 21 April 2023 data cut-off was 25.5 months. Members also reviewed the findings of an updated analysis from May 2024.

8.18.1. The Committee noted that the findings from the EPCORE NHL-1 study were promising, particularly given the extent to which participants had been heavily pre-treated. Members noted findings from the April 2023 data cut [95%CI]; ORR 61.9% [53.3-70.0]; CR 40.3% [32.1-48.9]; and median OS 19.4 months [11.7-27.7]. The Committee noted that 91% of those who achieved a CR were alive at 9 months, and considered those who achieved a CR on epcoritamab to have particularly favourable outcomes. Overall, the Committee considered for those who achieved a CR, the treatment effect was likely to be durable.

8.18.2. The Committee considered epcoritamab to be well tolerated based on the available evidence. Members noted that a large proportion of participants experienced CRS (49.6%), but most cases were of mild severity (grade 1 and 2).

8.18.3. The Committee considered the findings of EPCORE-NHL 1 were supported by the findings of a comparable single country (Japan) phase I/II study ECHORE NHL-3 (Izutsu et al. Int J Clin Oncol. 2025;30:1631-40). The committee noted that 47% of participants achieved a complete response, of whom 53% remained in remission at 3 years. The Committee noted the validated tools used to record patient reported outcomes, and noted that 90% of patients reported positive impacts on daily activities and 38.9% of patients reported positive impacts on physical functioning

8.18.4. The Committee discussed the quality of the EPCORE NHL 1 & 3 studies and considered that the available evidence was limited by a lack of a phase III investigation. Members noted that EPCORE NHL-3 was conducted in a single country, with a small number of participants (n=36), however, both studies suggested that epcoritamab was associated with a meaningful treatment effect. The Committee considered the evidence to be generalisable to the New Zealand context.

8.19. The Committee noted a matched adjusted indirect comparison (MAIC) was included in the epcoritamab submission that compared OS associated with epcoritamab from a subgroup of EPCORE NHL-1 (n=86, no prior CAR-T) to patients receiving chemoimmunotherapy from SCHOLAR-1, a retrospective study with pooled data from two Phase 3 trials and two observational cohorts (Crump et al. Blood. 2017;130:1800-8). The estimated OS HR was 0.512 (95% CI: 0.378 – 0.693) before adjustment and 0.344 (95% CI: 0.203, 0.582) after adjustment in favour of epcoritamab.

8.19.1. The Committee discussed the quality of the MAIC, and considered the findings should be interpreted with caution given the inherent uncertainty with

unanchored indirect comparisons. The Committee considered that while the findings suggest a survival advantage in favour of epcoritamab, the magnitude of the difference in treatment effect is uncertain. The Committee therefore considered that the more conservative unadjusted HR of 0.512 may be more appropriate for decision making.

8.19.2. The Committee noted that phase III direct comparative data would soon be available, and noted this evidence would be preferable to the MAIC.

8.20. The Committee discussed the use of Obinutuzumab as a pre-treatment for CRS, and noted the risk profile was acceptable and comparable to rituximab's.

8.21. The Committee noted that all the pivotal trials reviewed were conducted during the COVID pandemic and considered that each study presented manageable toxicity despite including infections and deaths related to COVID.

8.22. The Committee considered the risk profile associated with BiTEs as a class, noting that CRS and immune effector cell-associated neurotoxicity syndrome (ICANS) are class-specific adverse events requiring management through pre-medication, close monitoring, and hospitalisation in severe cases. The Committee considered that hospital-based management would require additional staff training in both monitoring and treatment.

8.23. The Committee considered that for the purpose of modelling, if an individual has maintained PFS out to three years, it was reasonable for them to be considered cured.

Suitability

8.24. The Committee noted that glofitamab and GemOx are administered by intravenous infusion. Members considered the burden this treatment schedule may place on individuals with RR-DLBCL and their whānau due to the time required for infusions and associated travel costs. The Committee discussed the existing strain on infusion resources in the health system and considered that funding glofitamab would further increase demand. The Committee noted that treatment would be administered for a maximum of 12 cycles.

8.25. The Committee noted that epcoritamab is administered as a subcutaneous injection. The Committee noted this route of administration is convenient, particularly for those who live in rural areas. The Committee discussed the ongoing maintenance phase for epcoritamab, in which the medicine is administered every 28 days until disease progression, as per the protocol in the EPCORE NHL-1 study. The Committee considered that ongoing treatment would be a burden for individuals and their families due to the need for ongoing follow-up appointments, and the time required to pick up the medication. The Committee considered in real world practice, individuals would be unlikely to remain on epcoritamab indefinitely in the absence of disease progression.

8.26. The Committee considered that exposure to glofitamab or epcoritamab can lead to CRS and ICANS, which may necessitate hospitalisation and coordination with an intensive care unit (ICU) for severe manifestations. The Committee considered that most of these complications are expected to be mild in severity (grade 1-2) and readily manageable. The Committee considered that severe manifestations could usually be managed with tocilizumab and would not always require admission to an ICU. The Committee considered that any facility administering glofitamab or epcoritamab would need to have immediate access to supportive medications such as tocilizumab to mitigate the risk associated with CRS, which would predominantly occur during the initial doses.

8.27. The committee noted that for the initial doses of either glofitamab or epcoritamab, premedication with corticosteroids, antihistamines, and antipyretics is required to reduce the severity of symptoms from potential manifestations of CRS. Members

noted for those receiving glofitamab, a single dose of Obinutuzumab is also administered to mitigate the risk of CRS.

Cost and savings

8.28. The Committee considered the estimated number of eligible patients provided in each submission to be reasonable.

8.29. The Committee noted that additional costs to the health system would be incurred with managing grade III toxicities, particularly severe manifestations of CRS.

8.30. The Committee considered that uptake of either treatment would likely be higher than the supplier estimates, with high uptake occurring immediately given the clear survival advantage over currently available treatments.

8.31. The Committee considered epcoritamab's indefinite maintenance phase would incur additional monitoring costs for patients that continued treatment.

8.32. The Committee considered there would be potential reductions in palliative chemoimmunotherapy use and associated hospitalisations if glofitamab and/or epcoritamab were funded.

8.33. The Committee noted that should a BiTE be funded for DLBCL, access to tocilizumab would need to be expanded for the management of CRS. The Committee noted that if glofitamab were funded, access to Obinutuzumab would also need to be expanded to enable its use as a pre-medication.

Funding criteria

8.34. The Committee considered glofitamab's special authority criteria should include a requirement for pre-treatment with Obinutuzumab, given that the risk profile was informed by STARGLO included this intervention. Pharmac staff note that this criterion is more directed toward appropriate clinical care rather than in defining the group for treatment and as such would be better captured in clinical advice resources.

Summary for assessment

8.35. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for glofitamab or epcoritamab for if it were to be funded in New Zealand for relapsed or refractory diffuse large B-cell lymphoma. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	**Glofitamab (≥2 line)** People with relapsed or refractory diffuse large B-cell lymphoma who have received **one or more** lines of systemic therapy and are unable to receive autologous stem cell transplant	**Epcoritamab (≥3 line)** People with relapsed or refractory diffuse large B-cell lymphoma who have received **two or more** lines of systemic therapy and are unable to receive autologous stem cell transplant.
Intervention	Glofitamab (12 cycles) + GemOx (first eight cycles only) Pre-treatment with Obinutuzumab (1 dose)	Epcoritamab Administered until disease progression or unacceptable toxicity
Comparator(s)	Rituximab gemcitabine oxaliplatin (R-GemOx) Treatment for up to 8 cycles	Rituximab in combination with gemcitabine, dexamethasone and cisplatin (R-GDP) Treatment for 7 cycles

Outcome(s)	PFS • STARGLO estimated median PFS of 13.8 months (95% CI: 8.7-20.5) for Glofit-GemOx and 3.6 months (95% CI: 2.5-7.1) for R-GemOx with a HR of 0.40 (0.28-0.57). OS • STARGLO estimated median OS of 25.5 months (95% CI: 18.3-NE) for Glofit-GemOx and 12.9 months (95% CI: 7.9-18.5) for R-GemOx with a HR of 0.62 (0.43-0.88)	PFS • EPCORE NHL-1 estimated median PFS was 4.4 months (95% CI: 3.0-8.8) OS • EPCORE NHL-1 estimated median OS was 19.4 months (95% CI: 11.7-27.7)
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.		

9. Momelotinib for intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF, with moderate to severe anaemia

Application

9.1. The Committee reviewed the supplier and consumer applications for momelotinib the treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF, with moderate to severe anaemia.

9.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

9.3. The Committee **recommended** that momelotinib be listed for the first-line treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF, with moderate to severe anaemia, **only if cost-neutral to ruxolitinib,** within the context of treatment of malignancy, subject to the following Special Authority criteria:

> Initial application - first-line treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF.
> Applications only from a haematologist. Approvals valid for 12 months.
> All of the following:
> 1. The patient has primary myelofibrosis or post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis; and
> 2. Disease has a risk classification of intermediate-1, intermediate-2 or high-risk myelofibrosis according to either the International Prognostic Scoring System (IPSS), Dynamic International Prognostic Scoring System (DIPSS), or the Age-Adjusted DIPSS; and
> 3. Either
> 3.1.1. Patient has not previously received an alternative JAK inhibitor for MF; or
> 3.1.2. Patient has an intolerance to an alternative JAK inhibitor based on a non-haematological cause (eg allergic reaction to ruxolitinib, life-threatening rash, or liver function derangement).
>
> Renewal
> Applications only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months.
> 1. The treatment remains appropriate and the patient is benefiting from treatment.

9.4. In making this recommendation, the Committee considered

- The available evidence suggests that ruxolitinib and momelotinib offer similar health benefits and risks in a first line setting.

- There is insufficient evidence to suggest a difference in survival or health-related quality of life between the treatments.
- A reduction in number of blood transfusions for individuals in the first 24 weeks of treatment compared with ruxolitinib.

9.5. The Committee considered that if momelotinib were funded for first-line treatment of myelofibrosis as an alternative to ruxolitinib, a criterion regarding intolerance (ie patient has an intolerance to an alternative JAK inhibitor based on a non-haematological cause [eg allergic reaction, life-threatening rash, or liver function derangement not improved with dose reduction]) could similarly be applied to the funding criteria for ruxolitinib.

9.6. The Committee **recommended** that momelotinib be listed for the second-line treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera MF or post-essential thrombocythaemia MF, with moderate to severe anaemia, with a **high priority** within the context of treatment of malignancy, subject to the following Special Authority criteria:

Initial application
Applications only from a haematologist. Approvals valid for 12 months.
All of the following:
1. The patient has primary myelofibrosis or post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis; and
2. Disease has a risk classification of intermediate-1, intermediate-2 or high-risk myelofibrosis according to either the International Prognostic Scoring System (IPSS), Dynamic International Prognostic Scoring System (DIPSS), or the Age-Adjusted DIPSS; and
3. Patient has severe disease related symptoms that are resistant or refractory to an alternative JAK inhibitor.

Renewal
Applications only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months.
1. The treatment remains appropriate and the patient is benefiting from treatment.

9.7. In making this recommendation the Committee considered:

- The high health need of individuals whose disease has progressed during or following ruxolitinib treatment
- The lack of second line treatment options for MF
- Momelotinib provides a health benefit in the second line setting compared with historical control data and current standard of care.

Discussion

Māori impact

9.8. The Committee discussed the impact of funding momelotinib for the treatment of intermediate or high-risk primary myelofibrosis (MF), post-polycythaemia vera (PV) MF or post-essential thrombocythaemia (ET) MF, with moderate to severe anaemia on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee noted data from the New Zealand Cancer registry for primary MF that reported of 152 people, 9.9% were Māori. The Committee noted the age of diagnosis was approximately 5-10 years younger in Māori compared with New Zealand European. The Committee considered the data suggested an inferior overall survival in Māori, however the number of individuals included in the registry is too small to be definitive.

Populations with high health needs

9.9. The Committee discussed the health need(s) of intermediate or high-risk primary MF, post-PV MF or post-ET MF, with moderate to severe anaemia among Māori, Pacific

peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 to have high health needs. The Committee discussed the impact of funding momelotinib and considered:

9.9.1. A New Zealand MF registry (Varghese et al. Curr Oncol. 2021;28:1544-57) reported that of 152 people approximately 6.6% were Pacific people. The Committee noted the age of diagnosis was approximately 5-10 years younger in Pacific people compared with New Zealand European. The Committee considered the data suggested an inferior overall survival in Pacific People, however the number of individuals included in the registry is too small to be definitive.

9.9.2. Individuals from rural areas may have to travel further to access transfusion support for anaemia. This would include additional time away from whānau, as well as travel expenditure and time away from paid employment.

Background

9.10. The Committee noted ruxolitinib is currently funded for the treatment of MF for low-risk intermediate-1, high-risk and intermediate-2 disease. No other Pharmaceutical Schedule funding applications for specific treatments for MF have been considered by Pharmac.

Health need

9.11. The Committee noted the health need of individuals has been considered by PTAC November 2016, Haematology Subcommittee November 2017 and PTAC May 2018.

9.12. The Committee considered secondary MF in the setting of a prior myeloproliferative neoplasm describes individuals with ET and PV who develop disease progression to MF, post PV-MF and post ET-MF.

9.13. The Committee noted that MF mainly affects older adults with a median age of ≥65 years at diagnosis (ruxolitinib data for release under OIA. October 2024).

9.14. The Committee reviewed data from the New Zealand Cancer registry data for primary MF (Varghese et al. Curr Oncol. 2021;28:1544-57). The Committee noted the registry was limited to 152 people, with 9.9% Māori and 6.6% Pacific people. The Committee noted the age of diagnosis was approximately 5-10 years younger in Māori and Pacific people compared with New Zealand European. The Committee considered the data suggested an inferior overall survival in both Māori and Pacific People, however the number of individuals included in the registry is too small to be definitive.

9.15. The Committee considered that the only curative therapy for MF is an allogenic stem cell transplant.

9.16. The Committee considered individuals who are transplant eligible would receive ruxolitinib (a Janus kinase [JAK] inhibitor) to maintain disease control, performance status and quality of life for the individual.

9.17. The Committee considered ruxolitinib would be used instead of hydroxyurea in clinical practice, based on the COMFORT trials. The Committee considered PEG-interferon (PEG-IFN) had a low efficacy in INT-2 or high-risk MF individuals, with the main efficacy in low-risk individuals. Therefore, the main treatment would be ruxolitinib for all individuals who are INT-1 symptomatic, INT-2 or high-risk MF.

9.18. The Committee considered that a haemoglobin level of <100g/l is prognostic, and the individual is more likely to need a JAK inhibitor therapy and have either INT-2 or high risk disease. The Committee noted that haemoglobin is a dynamic measure, with levels known to decrease as MF progresses and following ruxolitinib treatment. However, the Committee considered patient need could not be accurately determined by a precise haemoglobin level or threshold.

9.19. The Committee noted that ruxolitinib is associated with worsening anaemia in the first 12 weeks of initiating treatment, which improves and stabilises by 24 weeks in the majority of patients. This effect was observed in the COMFORT II clinical trial in 46% of individuals. The Committee considered overall this does not affect long term outcomes, with a median haemoglobin level of 110g/l at four years.

9.20. The Committee considered the highest unmet health need is for individuals who require second line treatment following ruxolitinib treatment where disease progresses or is refractory to treatment, especially in individuals who are not eligible for a transplant. The Committee considered that disease progression on ruxolitinib can be identified by increase in spleen size, new or worsening 'B symptoms' (night sweats, weight loss etc) and persistent or progressive clinically significant anaemia.

Health benefit

9.21. The Committee noted momelotinib is a JAK inhibitor that also inhibits ACVR2.

First line

9.22. The Committee noted the SIMPLIFY-1 study (Mesa et al. J Clin Oncol. 2017;35:3844-50), a phase III trial randomised, double-blind, multicentre trial that compared momelotinib and ruxolitinib in JAK inhibitor-naïve patients with INT-1, 2 or high-risk MF.

9.22.1. The Committee noted the endpoints were measured at 24 weeks. The Committee considered there was no difference in the primary endpoint (≥35% reduction in spleen volume (SRR)) compared with ruxolitinib at 24 weeks. The Committee noted there was a greater improvement in total treatment score >50% (TSS) in individual treated with ruxalitinb compared to momelotinib.

9.22.2. The Committee noted that momelotinib had a greater transfusion independence rate (TI-R) however considered the need for transfusions due to worsening anaemia were an expected side effect of ruxolitinib that improved and stabilised by 24 weeks.

9.22.3. The Committee noted the primary endpoint of SRR reached non-inferiority, however 50% reduction in TSS did not.

9.23. The Committee considered the SIMPLIFY-1 trial was generalisable to the New Zealand context. The Committee considered that the available evidence suggests that ruxolitinib and momelotinib offer similar health benefits and risks in a first-line setting. The Committee considered there is insufficient evidence to suggest a difference in survival or health-related quality of life between the treatments.

9.24. The Committee considered the 24 week follow up period of SIMPLIFY-1 favours momelotinib, due to the mechanism of action of ruxolitinib. The Committee considered that it was common for ruxolitinib to be associated with anaemia requiring transfusions in the first six months, and for this to largely improve and stabilise following this period. The Committee considered that it was therefore not surprising for momelotinib to be associated with higher TI-R in the first six months, and that in the absence of longer-term data, it was not reasonable to assume that this improvement in the rate of TI-R would be sustained past this period.

Second line

9.25. The Committee noted the SIMPLIFY-2 study (Harrison et al. Lancet Haematol. 2018;5:e73-81) a phase III, randomised, open-label, multicentre trial that compared momelotinib vs best available therapy (BAT), including ruxolitinib, in JAK inhibitor-experienced patients.

9.25.1. The Committee noted individuals must have been exposed to ruxolitinib for at least 28 days and required either a red blood cell transfusion or dose reduction to less than 20mg twice a day with at least one of: grade 3 thrombocytopenia or anaemia with palpable spleen of at least 5cm. The Committee considered

both of these side effects are commonly experienced on ruxolitinib treatment. The Committee noted up to 19% of individuals in the trial had less than 12 weeks of ruxolitinib treatment.

9.25.2. The Committee noted 89% of individuals in the BAT arm received ruxolitinib, with 25% of individuals receiving a ruxolitinib dose of <5mg twice a day. The Committee considered this dose was below the therapeutic range and not commonly used in clinical practice.

9.25.3. The Committee noted momelotinib was not superior to BAT in reducing spleen volume at 24 weeks (7% momelotinib vs 6% BAT), however did show a greater improvement in TSS (26% momelotinib vs 6% BAT, nominal p=0.0006) and TI-R (43% momelotinib vs 21% BAT, nominal p=0.0012). The Committee considered these results are in line with worsening anaemia associated with ruxolitinib treatment (as received by most in the control arm) that improves and stabilises by 24 weeks.

9.25.4. The Committee considered that while the SIMPLIFY-2 trial provided evidence of a benefit from momelotinib in patients previously treated with ruxolitinib, it was not ideal as a means of defining a group of patients resistant or refractory to ruxolitinib in the New Zealand context, noting that many of the people in the comparator arm were continuing on their first-line treatment. The Committee therefore considered that the SIMPLIFY-2 trial should also not be used to reflect the dosage, or outcomes of people refractory to ruxolitinib.

9.26. The Committee noted the MOMENTUM trial (Verstovsek et al. Lancet. 2023; 401:269-280); a phase III, randomised, double blind, multicentre trial that compared momelotinib vs danazol for 24 weeks in JAK inhibitor-experienced anaemic patients. The Committee noted that the trial required participants to be symptomatic and have an Hb of less than 100 g/L for enrolment. The Committee considered the design of the trial was more clinically relevant to consideration of second line momelotinib, with participants having essentially ruxolitinib-refractory disease. Both treatment arms had a median JAK inhibitor exposure of >100 weeks (minimum 90 days or at least 28 days if requiring more than four RBC transfusions).

9.26.2. The Committee noted SRR and TSS improvement was greater for momelotinib compared with danazol.

9.26.3. The Committee noted the TI-R was non-inferior between the two treatments, with a superior rate of zero transfusions to week 24. The Committee considered danazol is routinely used to resolve anaemia associated to MF, however, is not funded in New Zealand.

9.26.4. The Committee noted that overall, regardless of randomisation during the double-blind randomised period, approximately 60% of individuals in the trial were alive at 60 weeks of treatment. The Committee considered overall this data suggested momelotinib provided health benefit to individuals as a second line treatment.

9.26.5. The Committee considered that the outcomes among people treated with momelotinib in the MOMENTUM trial to be applicable to the New Zealand context. The Committee considered that outcomes are typically poor for people with ruxolitinib-refractory disease, with the Committee estimating that based on their clinical experience, survival may be approximately 14-16 months with standard treatments. The Committee therefore considered the results reported in MOMENTUM to be indicative of an improvement in outcomes, and that it was reasonable to assume that momelotinib would likely be associated with an improvement in survival in those with disease refractory to ruxolitinib. However, the Committee considered the extent of overall survival improvement was highly uncertain.

9.26.6. The Committee considered that the outcomes observed in the comparator arm of MOMENTUM were not generalisable to New Zealand due to the high degree of crossover. The Committee noted that people in the danazol arm were able to receive momelotinib after 24 weeks, and that the rate of crossover was high. The Committee considered that the results beyond this 24-week time point should be interpreted with caution and did not reflect the outcomes that would be expected in New Zealand.

9.27. The Committee was made aware of observational evidence that may indicate survival outcomes for people who are refractory to first-line ruxolitinib:

- Newberrry et al. Blood 2017;130: 1125-31
- Palandri et al. Cancer 2020;126: 1243-52

First and second lines of treatment

9.28. The Committee noted Mesa et al. Leukemia. 2022;36:2261-8 that reported the results of the open label extended access protocol from the SIMPLIFY-1 and -2 trials.

9.28.1. The Committee noted the SIMPLIFY-1/2 trials reported there was no difference in overall survival based on previous JAK inhibitor exposure status (SIMPLIFY-1 HR=1.02[0.73,1.43], SIMPLIFY-2 HR=0.98 [0.59,1.62]).

9.28.2. The Committee noted data that reported overall survival based on TI-R rate at 24 weeks. The Committee considered the individuals who experience poor TI-R rate on momelotinib treatment have a poor overall survival rate.

9.29. The Committee considered that observational studies of people after ruxolitinib treatment was likely to be the best evidence for outcomes with current treatments in New Zealand. The Committee further considered that those refractory to ruxolitinib would typically receive treatments such as steroids in combination with hydroxyurea.

9.30. The Committee considered that it would be appropriate to assume there would not be a significant change in the rate of death with momelotinib over time, and therefore the monthly rate of death observed in the momelotinib arm of MOMENTUM could be used to extrapolate beyond the trial duration. The Committee considered that MF is a long-term and incurable disease, and therefore the survival would not be expected to plateau significantly over time. The Committee further considered that while it is plausible that some people may develop resistance over time (based on their clinical experience of ruxolitinib), resistance takes several years to develop and therefore would be unlikely to occur in many of these patients due to the relatively poor prognosis of this group.

General

9.31. The Committee noted that there is currently a lack of evidence to support the use of second line ruxolitinib treatment following first line momelotinib treatment. The Committee considered that it may be appropriate to consider subsequent use of ruxolitinib only for cases of intolerance to first-line momelotinib, given the lack of evidence for ruxolitinib efficacy in the second line setting.

Suitability

9.32. The Committee considered a decrease in the need for transfusions in the first six months of treatment would benefit those who are required to travel long distances to receive transfusion support.

Cost and savings

9.33. The Committee considered the main health benefit of momelotinib in first line treatment compared to ruxolitinib is a decrease in the number of transfusions in the first 24 weeks. The Committee considered that the need for transfusions to manage anaemia was an expected side-effect in the first 24 weeks of ruxolitinib treatment,

and that this would be expected to improve and stabilise after 24 weeks. Therefore, the Committee considered that a reduction in transfusions with momelotinib (relative to ruxolitinib) should be assumed only for the first 24 weeks of treatment and that it would not be reasonable to assume any reduction in transfusions with momelotinib beyond this time point.

9.34. The Committee considered it was reasonable to assume no significant differences in the adverse events requiring healthcare treatment between ruxolitinib and momelotinib treatment. The Committee considered that the SIMPLIFY-1 trial suggested ruxolitinib provided better early symptom control than momelotinib in first line treatment, but that MF symptoms rarely require hospitalisation. The Committee therefore considered that the difference in symptom management would be unlikely to have a meaningful impact on the rate of health resource utilisation. However, the Committee considered that this would have some impact on health-related quality of life.

9.35. The Committee noted Tefferi et al that Mayo Clin Proc. 2012 ;87:25-33. reported a retrospective analysis of 1000 patients with MF. The Committee noted that while anaemia was reported in 38% of individuals, it considered it would be higher in the INT-2 and high-risk groups. The Committee considered that as the data was collected from 1977 to 2011, the long-term data should be interpreted with caution as individuals would not have had access to JAK inhibitor treatment and therefore it does not reflect the current standard of care.

9.36. The Committee considered the reported dosing from SIMPLIFY-1 trial to be the most appropriate for use in modelling. The Committee considered that the sub-therapeutic dosing of ruxolitinib in the SIMPLIFY-2 trial does not reflect clinical practice, where dosing is reduced following adverse events, before being rapidly increased to the maximal tolerated dose.

9.37. The Committee considered it would not be appropriate to restrict JAK inhibitor therapy to those that are ineligible for haematopoietic stem cell transplant.

Funding criteria

9.38. The Committee considered the existing Special Authority criteria for ruxolitinib should be adjusted to combine the IPSS/DIPSS classifications and remove the need for individuals to have severe disease related symptoms that are resistant, refractory or intolerant to available therapy.

9.39. The Committee considered it would be appropriate for the momelotinib Special Authority criteria to match the current ruxolitinib criteria in the first line setting.

9.40. The Committee considered that, as anaemia is expected within the first 24 weeks of treatment with ruxolitinib and can be managed with transfusions, intolerance to ruxolitinib should be defined as an intolerance based on a non-haematological cause (eg allergic reaction to ruxolitinib, life-threatening rash, or liver function derangement not improved with dose reduction).

9.41. The Committee considered for momelotinib treatment; it was not necessary to specify a haemoglobin level to target those with the greatest need and that anaemia should be removed as a criterion given that the IPSS and DIPSS risk stratification takes this into account. The Committee considered that this would not affect the population size who would receive treatment.

9.42. The Committee considered it would be appropriate for individuals whose disease is refractory to, or progresses on, ruxolitinib to receive momelotinib in second line treatment. However, the Committee considered it would only be appropriate to consider funding subsequent use of ruxolitinib for cases of intolerance to first-line momelotinib, given the lack of evidence for second-line efficacy of ruxolitinib. The Committee noted that a criterion regarding momelotinib intolerance could be applied to the funding criteria for ruxolitinib to enable this.

Summary for assessment

9.43. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for momelotinib if it were to be funded in New Zealand for primary myelofibrosis or post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	*1st line:* People with primary myelofibrosis or post-polycythaemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis Patients must be JAK-inhibitor naive	*2nd line:* People with primary myelofibrosis or post-polycythaemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis Patients must be refractory or intolerant to a 1st line JAK inhibitor
Intervention	Momelotinib 200 mg orally once daily, with dosing adjusted as needed based on tolerability and platelet count	
Comparator(s)	Ruxolitinib (10, 15, 20 mg) orally twice-daily, with dosing adjusted as needed based on the platelet count and tolerability	Best alternative therapy – typically steroids with hydroxyurea Mix of current treatments likely to be similar to those in the comparator arm of the COMFORT-I and COMFORT-II trials of ruxolitinib in a 1L setting
Outcome(s)	*Health-related quality of life and survival* No difference in health-related quality of life, survival, or management of MF between momelotinib and ruxolitinib, based on SIMPLIFY-1 *Blood transfusions* Reduced requirement for blood transfusions in the first 24 weeks of treatment, compared to ruxolitinib Likely no difference in blood transfusions beyond 24 weeks, compared to ruxolitinib	*Overall survival* Likely improved survival with momelotinib compared with current treatments, based on 24-week results of MOMENTUM and comparison to observational cohorts (e.g.Newberrry et al. Blood 2017;130: 1125-31; Palandri et al. Cancer 2020;126: 1243-52)
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.		