PHARMAC
TE PĀTAKA WHAIORANGA

Specialist Advisory Committees
Objective advice to Pharmac

Record of the Cancer Treatments Advisory Committee Meeting held on 20 March 2026

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
Allanah Kilfoyle
Chris Frampton
Lochie Teague
Matthew Strother
Oliver Brake
Richard Isaacs
Scott Babington
Vidya Mathavan

Apologies
Alice Minhinnick

Observer – Invited expert
Helen Evans (Chair, Rare Disorders Advisory Committee)

2. Summary of recommendations

	Pharmaceutical and Indication	Recommendation
7.2	Hexylaminolevulinate hydrochloride (Hexvix) for diagnostic detection of bladder cancer	Decline
9.1	Pertuzumab with trastuzumab (PHESGO), subcutaneous, for adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence in combination with chemotherapy	Decline
9.2	Pertuzumab, intravenous, for adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence in combination with trastuzumab and chemotherapy	Decline
10.1	Pertuzumab and trastuzumab (PHESGO) for HER2-positive metastatic or locally recurrent unresectable breast cancer be widened to individuals with an ECOG status score 2-3	Medium priority
11.4	Belzutifan for the treatment of von-Hippel Lindau disease	Medium priority

12.3	Eltrombopag access be widened to the first-line treatment of severe aplastic anaemia, within the context of haematology treatments	High priority
12.4	Eltrombopag access be widened to the second-line treatment of relapsed/refractory severe aplastic anaemia, within the context of haematology treatments.	High priority

These recommendations were made within the context of treatments of malignancy, unless otherwise stated in the above table.

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.'

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. Record of CTAC meetings held Friday 12 September and Thursday 9 October 2025

5.1. The Committee reviewed the records of the Cancer Treatments Advisory Committee meetings held on 12 September and 9 October and agreed that the records be accepted.

6. Pharmac Update including procurement updates

6.1. The Committee noted the Pharmac Update.

6.2. The Committee acknowledged the recent staff updates and noted the ongoing recruitment.

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

6.4. The Committee noted the following organisational updates:

6.4.1. Organisational vision and strategy

6.4.2. Equity Policy updated in December 2025

6.4.3. Consultation for the Exceptional circumstances framework review

6.4.4. Recruitment for new membership is underway for the Committee

6.5. The Committee noted the decision not to decline applications with lower OFI ranking.

7. Matters Arising: Hexylaminolevulinate hydrochloride (Hexvix) for diagnostic detection of bladder cancer

7.1. The Committee discussed a funding application for hexylaminolevulinate hydrochloride (Hexvix) for diagnostic detection of bladder cancer considered by the Cancer Treatments Subcommittee (CaTSoP, now CTAC) in April 2018. At the time the Committee deferred making a recommendation pending further information. Pharmac reached out to NZ Urology Clinical Directors' Group to see if there is still interest in pursuing the application.

7.1.1. The Clinical Directors' Group advised they do not seek to pursue the application and advised they would like to retire the application.

7.1.2. The Committee noted the advice of the Clinical Directors' Group and agreed there is no additional need to pursue this application.

7.2. The Committee **recommended** the application for hexylaminolevulinate hydrochloride (Hexvix) for diagnostic detection of bladder cancer **be declined**.

8. Matters arising – Requests for ECOG status widening – review approach

Discussion

Background

8.1. The Committee noted that the Eastern Cooperative Oncology Group performance status (ECOG PS) scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity and physical ability.

8.2. The Committee noted that ECOG PS is widely used in clinical trial inclusion criteria and is also used in clinical practice to assess patients' baseline performance status, suitability for treatment and response to treatment.

8.3. The Committee noted that Pharmac has incorporated ECOG PS into funding eligibility criteria for selected cancer treatments, with the intention of targeting funding to people who are representative of the clinical trial population on which the funding decision is based. This approach is expected to increase the likelihood that funding is allocated to individuals for whom evidence demonstrates a treatment benefit and for whom the economic analysis used in the health technology assessment is expected to be generalisable.

8.4. The Committee noted that Pharmac currently funds 30 cancer treatments across 51 indications which have funding eligibility criteria that include ECOG PS, with the most common ECOG PS range being 0-2.

8.5. The Committee noted international health technology assessment approaches to incorporating ECOG PS into reimbursement criteria have varied. Australia's Pharmaceutical Benefits Advisory Committee (PBAC) and Canada's Drug Agency (CDA) often include ECOG PS eligibility criteria in their recommendations, while the United Kingdom's National Institute for Clinical Excellence (NICE) and France's National Authority for Health (HAS) rarely include ECOG PS eligibility criteria in their recommendations.

8.6. The Committee noted that Pharmac has received requests from clinician and consumer stakeholders to widen access to specific medicines for people with poorer ECOG PS than those included in funding eligibility criteria.

8.7. The Committee noted that Pharmac sought the Committee's advice on:

8.7.1. The appropriateness and effectiveness of using ECOG PS in cancer treatment funding eligibility criteria.

8.7.2. The impact of widening ECOG PS criteria to allow funding for people with poorer performance status.

8.7.3. Pharmac's general approach to considering requests to widen access to cancer treatments for people with poorer performance status.

Evidence appraisal

8.8. The Committee noted a cross-sectional study investigating the performance status eligibility requirements of clinical trials that led to FDA approval of cancer treatments between 2009 to 2023 (Lannantuono et al. European Journal of Cancer. 2025 Jun 26:115589).

8.8.1. The Committee noted that of the 283 trials reviewed between 2009 to 2023, less than 5% included participants with ECOG PS of 2 or greater.

8.8.2. The Committee noted that the low recruitment of participants with ECOG PS of 2 or greater limits the generalisability of trial results to people with poorer performance status.

8.9. The Committee noted the retrospective cohort study examining associations between ECOG PS and adverse outcomes in a real world Northern Californian community oncology population receiving intravenous (IV) systemic therapy (Kumar et al. Journal of National CCN. 2024 Apr 23;22).

8.9.1. The Committee noted that ECOG PS was found to be independently associated with increased risk of emergency department visits, hospitalisations, and mortality.

8.10. The Committee noted two retrospective cohort studies evaluating the impact of ECOG PS on clinical outcomes in patients with non-small cell lung cancer (NSCLC) treated with immune checkpoint inhibitors (ICIs) (Meyers et al. JTO Clinical and Research. 2023 Apr 1;4(4):100482) (Sehgal et al. JAMA. 2021 Feb 11;4(2):2037120).

8.10.1. The Committee noted in the study conducted by Meyers et al., patients with poor performance status (ECOG PS ≥2) had inferior median overall survival (mOS), time-to-treatment failure (TTF) and objective response rate (ORR) compared to patients with favourable performance status (ECOG PS <2).

8.10.2. The Committee considered that a higher proportion of patients in the poor performance status group had liver and bone metastases and received treatment in second or later lines of therapy compared with the favourable performance status group.

8.10.3. The Committee noted similar results from the study by Sehgal et al., with patients with poorer performance status (ECOG PS ≥2) exhibiting shorter median progression free survival (mPFS) and mOS compared to those with ECOG PS <2.

8.11. The Committed noted an analytical cross-sectional study evaluating the relationship between clinician-rated ECOG PS and patient reported health-related quality of life (HRQoL) in men with metastatic hormone-naïve prostate cancer in Nigeria (Nnabugwu et al. Health and Quality of Life Outcomes. 2024 Dec 24;22(1):111).

8.11.1. The Committee noted the study reported a correlation between HRQoL questionnaire domains and ECOG PS; however, considered these results were not generalisable to practice in New Zealand due to the difference in patient quality of life between practice environments.

8.12. The Committee noted a meta-analysis investigating the impact of including ECOG PS 2 participants on the efficacy and safety outcomes of pivotal phase III cancer clinical trials, compared with those with ECOG PS ≤1 (Lannantuono et al. ESMO Open. 2026 Feb 1;11(2):106065).

8.12.1. The Committee noted that in meta-regression analyses, no significant associations were found for efficacy outcomes. However, a higher proportion of ECOG PS 2 participants was significantly associated with an increased risk of serious adverse event or adverse event-related deaths, and treatment discontinuations.

8.13. Th Committee commented that there is emerging evidence from machine learning-based trial emulation studies investigating the generalisability of oncology trial results to real-world outcome data. The Committee commented that results from these studies suggest real-world outcomes become more representative of trial outcomes when real-world patient characteristics are more representative of trial participants.

General

8.14. The Committee considered that the application of ECOG PS in funding eligibility criteria is subjective and not strictly adhered to in practice. The Committee considered that ECOG PS criteria is less likely to be adhered to when treating patients' whose poor performance status is thought to be disease related and expected to be reversible following treatment.

8.15. The Committee considered that treatment benefit and safety exhibited from pivotal clinical trials is not generalisable to those with poorer ECOG PS due to trial recruitment excluding those with poor performance status.

8.16. The Committee considered that, in general, those with better performance status are likely to obtain greater benefits from cancer treatments and tolerate them better compared to those with poorer performance status.

8.17. The Committee considered that people with poorer performance status may still experience a treatment benefit from cancer treatments; however, the effect size is likely to be reduced compared with those with more favourable performance status.

8.18. The Committee considered that, overall, including people with poorer ECOG PS in cost utility analyses may result in poorer cost utility of cancer treatments.

8.19. The Committee considered that widening access to cancer treatments for people with poorer ECOG PS would likely increase the number of people accessing treatment. However, noted that as ECOG PS criteria may not strictly be adhered to in practice, a proportion of this group may already receive currently funded treatments.

8.20. Overall, the Committee considered that as some patients with poorer ECOG PS may still receive a treatment benefit from funded cancer treatments, and ECOG PS criteria are not strictly adhered to in practice, there is a desire to remove ECOG PS from cancer treatment eligibility criteria. However, it was noted that this would likely impact the cost utility and budget impact of cancer treatments, which Pharmac would need to consider.

9. Pertuzumab and trastuzumab: adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence in combination with chemotherapy

Recommendations

9.1. The Committee **recommended** that subcutaneous pertuzumab with trastuzumab (PHESGO) for adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence in combination with chemotherapy **be declined**.

9.2. The Committee **recommended** that intravenous pertuzumab for adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence in combination with trastuzumab and chemotherapy **be declined**.

9.3. In making this recommendation the Committee considered:

- the minimal clinically meaningful benefit observed in the APHINITY trial
- the unmet health need in this population is largely addressed by the other funded treatments in this setting.

Discussion

9.4. The Committee noted that Pharmac consulted on a proposal to fund a subcutaneous (SC) formulation of pertuzumab and trastuzumab (PHESGO) for metastatic breast cancer in October 2025. This was subsequently funded in December 2025.

9.5. The Committee noted as part of the consultation, feedback was received on an application for PHESGO for the adjuvant treatment of individuals with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer at high risk of recurrence in combination with chemotherapy.

9.6. The Committee noted the application was previously reviewed by PTAC in November 2022 and deferred '*pending the final overall survival analysis of the APHINITY study planned to be conducted in approximately 2024*'.

9.7. The Committee noted that supporting evidence was provided by the Breast Cancer Aotearoa Coalition and Breast Cancer Foundation New Zealand as part of the consultation feedback.

9.8. The Committee considered the BCIRG 006 trial identified the individuals with HER2-positive, invasive, high-risk, node-negative or node-positive adenocarcinoma with an unmet health need. The Committee considered these individuals still have room for improvement in response (prolonged progression free or overall survival benefit) to adjuvant trastuzumab and chemotherapy treatment (Slamon et al. N Engl J Med 2011;365:1273-83).

APHINITY trial

9.9. The Committee noted that disease-free survival (DFS) was statistically significantly improved at 45 months for individuals who had node positive disease, however not in the intention to treat (ITT) population. The overall survival (OS) was not statistically significantly improved (von Minchwitz et al. N Engl J Med 2017;377:122-31).

9.10. The Committee noted the DFS was statistically significantly improved at 60 months for the ITT population. The OS was not statistically significantly improved (Loibl et al. J Clin Oncol. 2024;42;3643-51.).

9.11. The Committee noted the OS was statistically significantly improved for the ITT population at 135.6 months (Loibl et al. 2025).

9.12. The Committee considered the toxicity profile observed in the trial was similar to that observed in clinical practice.

9.13. The Committee noted that adjuvant trastuzumab and chemotherapy treatment was the comparator in the APHINITY trial (Loibl et al. ESMO OPEN; 2025;10; S4, 105112).

9.14. The Committee noted there was a protocol amendment following a faster than expected recruitment of individuals who were node negative and a reduced number of recruitment of individuals who were node positive. The Committee noted the amendment prevented the recruitment of node-negative patients and led to a delay in the timings of planned assessments. The Committee considered it was likely this did not have a significant effect on the results of the trial.

9.15. The Committee noted the Canada Drug Agency recommendation noted that the protocol amendment may have been overpowered due to an over recruitment of patients who were node positive.

9.16. Overall, the Committee considered the trial was of good quality, however considered whilst there was a statistically significant improvement in the ITT population, this may not be considered clinically meaningful in practice.

Overall Considerations

9.17. The Committee noted that the European Society for Medical Oncology (ESMO) Magnitude of Clinical Benefit Scale (MCBS) scored this treatment a C, which the Committee considered suggested marginal benefit.

9.18. The Committee noted Pharmac sought feedback from the Breast Cancer Special Interest Group that suggested the proposal be declined due to limited clinical benefit (invasive disease-free survival benefit only).

9.19. The Committee considered if pertuzumab and trastuzumab, either in SC or intravenous (IV) formulations were available, the majority would receive neoadjuvant treatment. The Committee considered in the adjuvant setting, those who did not experience a complete response would receive trastuzumab emtansine. For those that did experience a complete response individuals would receive trastuzumab alone.

9.20. The Committee considered a small percentage (≤10%) would receive adjuvant trastuzumab alone. The Committee considered this would typically be individuals with tumours that are at risk of being unresectable if they progress during neoadjuvant treatment.

9.21. The Committee considered that the results of the APHINITY trial are not generalisable to individuals who receive neoadjuvant trastuzumab monotherapy. The Committee considered that these individuals would receive a lower efficacy from the monotherapy, compared to trastuzumab in combination with pertuzumab.

9.22. The Committee considered it was uncertain if pertuzumab in combination with trastuzumab would be as effective if administered as an adjuvant therapy alone, in comparison to neoadjuvant followed by adjuvant treatment. The Committee considered neoadjuvant therapy provided real time results on if the tumour was responding to treatment. The Committee considered individuals with an incomplete response would receive trastuzumab emtansine treatment, and this would confound analysis of the benefits of adjuvant therapy alone.

9.23. The Committee considered clinicians would be unlikely to use trastuzumab as a monotherapy in individuals who had achieved a complete response following neoadjuvant treatment and surgery.

9.24. The Committee considered it is unknown if retreatment in the metastatic setting with pertuzumab in combination with trastuzumab would provide health benefit in individuals who experience disease recurrence following completion of adjuvant treatment with the combination. The Committee considered most clinicians would consider retreatment with pertuzumab in combination with trastuzumab if there had been treatment free interval of ≥12 months.

9.25. The Committee considered it was reasonable to assume that the IV pertuzumab formulation used in combination with the trastuzumab IV formulation and SC combination formulation provided similar health benefit and safety profiles. The Committee considered the SC combination may not provide an adequate dose to some populations, for example those who are obese.

9.26. The Committee considered the SC formulation of the combination would reduce the nursing time associated with administering the treatment compared to the IV formulation. The Committee considered this would be significantly reduced if this treatment was provided in primary care, for example general practice, compared to the current infusion centre setting.

10. Pertuzumab and trastuzumab: Subcutaneous pertuzumab and trastuzumab (PHESGO) for the treatment of HER2-positive metastatic or locally recurrent unresectable breast cancer - feedback to consultation

Recommendation

10.1. The Committee **recommended** that pertuzumab and trastuzumab (PHESGO) for HER2-positive metastatic or locally recurrent unresectable breast cancer be widened to individuals with an ECOG status score 2-3 with a **medium priority** within the context of treatment of malignancy, subject to Special Authority criteria.

10.2. In making this recommendation the Committee considered:

- The unmet health need for this population
- This population would likely benefit from treatment

Background

10.3. The Committee noted Pharmac consulted on a proposal to fund a subcutaneous (SC) formulation of pertuzumab and trastuzumab (PHESGO) for metastatic breast cancer in October 2025. This was subsequently funded in December 2025.

10.4. The Committee noted feedback to the funding consultation was received in October 2025 from Breast Cancer Foundation NZ (BCFNZ), the Breast Cancer Aotearoa Coalition (BCAC) and the Breast Cancer Special Interest Group (BCSIG). Feedback sought to amend the funding criteria to include patients with a higher Eastern Cooperative Oncology Group (ECOG) performance status compared to the currently funded 0-1. The feedback varied, requesting inclusion of individuals with an ECOG score up to 2 or 3.

10.5. The supplier of PHESGO provided evidence of health benefit in this population to support the application.

10.6. The Committee noted the feedback also requested that there was no requirement for co-administration with a specific type of systemic therapy. The Committee noted following the consultation feedback, the current Special Authority criteria did not specify a specific chemotherapy partner. The Committee considered this was appropriate.

Discussion

10.7. The Committee considered that overall, the consultation feedback requested the inclusion of individuals who have poorer performance status as it is believed they would also benefit from treatment with pertuzumab in combination with trastuzumab.

10.8. The Committee considered that clinical trials typically excluded individuals with an ECOG≥1, due to historical trials reporting that poorer performance status was linked to a poorer response (Brufman et al. Anticancer Res. 1986;6:733-6). The Committee

considered therefore that there was a paucity of evidence to support the health benefit of treatments for individuals with an ECOG≥1 in clinical trials.

10.9. The Committee considered there was emerging trial evidence that included individuals with poorer performance status.

10.10. The Committee noted Wildiers et al. Lancet Oncol. 2018 Mar;19:323-36 that reported the results from EORTC 75111-10114, an open-label, randomised, phase 2 trial from the Elderly Task Force/Breast Cancer Group that enrolled 80 patients, with a WHO performance status of 0-3, and evaluated the effects of metronomic oral cyclophosphamide 50 mg per day plus trastuzumab and pertuzumab, or trastuzumab and pertuzumab alone.

10.10.1. The Committee noted that the trial allowed trastuzumab emtansine on progression, and the trial baseline characteristics were not well balanced with the control arm having an overall worse performance status at baseline.

10.11. The Committee considered the appropriate use of real-world evidence to determine statistically valid conclusions was evolving.

10.12. The Committee noted Polito et al JCO Oncol Pract. 2023;19:435-45 a retrospective analysis of patients in the FlatIron Health database. Of 1065 people included, 5.4% had an ECOG score of 2, and 1.4% had an ECOG>2. Median real world progression free survival in the subgroup of patients who met key CLEOPATRA eligibility criteria was 16.9 months which was numerically longer than that observed in the overall patient cohort.

10.13. The Committee noted the following studies:

- Del Lago et al. J Geriatr Oncol. 2022 ;13:582-93.
- Wildiers et al. Breast. 2022:64:100-11.

10.14. The Committee considered individuals who match the pivotal trial entry criteria are more likely to have a similar health benefit from treatment as the original trial when considering real world evidence.

10.15. The Committee considered a major confounder of real-world evidence was that many patients included in the trial data do not have ECOG recorded, and therefore may affect interpretation of the data with respect to performance status and efficacy.

10.16. The Committee considered some of the poorer outcomes from the studies may be due to the requirement for a taxane as part of the treatment which is poorly tolerated in this population.

10.17. The Committee considered there was no evidence of the effect of performance status on outcomes in those provided pertuzumab and trastuzumab compared with trastuzumab alone.

10.18. The Committee considered evidence suggests that taxanes or vinorelbine have similar efficacy in combination with human epidermal growth factor receptor 2 (HER2) directed therapies. The Committee considered vinorelbine has a more tolerable safety profile.

10.19. The Committee considered that the majority of individuals would receive vinorelbine in combination with pertuzumab and trastuzumab. The Committee considered a small population would not receive concomitant chemotherapy.

10.20. Overall, the Committee considered that the health benefits are likely similar for those with a poorer performance status (i.e. hazard ratios), however the absolute magnitude of benefit is likely less. The Committee considered this would be driven by both intolerance of adjunctive chemotherapy and underlying disease biology.

10.21. Overall, the Committee considered there was a lack of evidence to estimate the impact of performance status on the health benefit derived from treatment. The Committee noted Orcutt et al. Nat Med. 2025;31:457-65 that included performance status as part of a phenotype algorithm that reported a reduction in the magnitude of clinical benefit by 75% in the poor risk phenotype. The Committee noted this was a machine learning study.

10.22. The Committee considered there was a risk of additional treatment related toxicities in those who are already clinically frail.

10.23. The Committee considered clinicians would be unlikely to treat individuals with an ECOG>3, with many considering individuals who are bed bound as clinical frail, and not suitable for treatment.

10.24. The Committee considered anecdotal evidence that many individuals up to ECOG 3 had a high response rate to HER2 targeted treatment in combination with vinorelbine. The Committee considered there was significant clinical benefit in the group that responds to treatment.

10.25. The Committee considered it likely there would be a small increase in the number of individuals who would be treated compared to the currently funded population. The Committee considered the total number of individuals who may have HER2 positive breast cancer and would have an ECOG >1 would be less than 100 people. This is based on the number of annual deaths due to breast cancer which are assumed to be HER2 positive; these patients would be assumed to have an ECOG >1 within that year.

10.26. However, the Committee considered in clinical practice, ECOG scoring was variable, and open to interpretation by the clinician. Therefore, it was reasonable to assume the majority of the individuals who were ECOG ≤3 may already be accessing the treatment.

11. Belzutifan for von-Hippel Lindau disease

11.1. Welcome and introduction

11.1.1. The Chair welcomed Dr Helen Evans, Chair of the Rare Disorders Advisory Committee. Dr Evans attended the meeting as an Observer for the discussion of belzutifan for von-Hippel Lindau disease to provide background context of the application which has previously been discussed by the Rare Disorders Advisory Committee in 2024.

11.1.2. The Committee acknowledged that Pharmac staff had invited input from several international experts who treat people with von-Hippel Lindau disease and were not able to secure their attendance as an Observer – Invited Expert at the meeting.

Application

11.2. The Committee reviewed the application for belzutifan for the treatment of von Hippel-Lindau (VHL) disease

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

Recommendation

11.4. The Committee **recommended** that belzutifan for the treatment of von-Hippel Lindau be funded with a **medium priority** within the context of treatment of malignancy subject to the following Special Authority criteria:

Initial application – (von Hippel-Lindau disease) from a medical oncologist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:
1. Patient has a confirmed diagnosis of von Hippel-Lindau disease; and
2. Either
    2.1 Patient has associated renal cell carcinoma or pancreatic neuroendocrine tumours with a tumour size of 2 cm - ≤3 cm or
    2.2 Smaller tumours of any type showing a ≥20% increase in size over 12/12 or
    2.3 Patient has von Hippel-Lindau disease associated central nervous system haemangioblastomas and
3. There is no evidence of metastatic disease; and
4. Patient has an ECOG performance status of 0-2; and
5. Patient has not received any prior systemic anti-cancer therapy

Renewal application – (von Hippel-Lindau disease) from a medical oncologist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:
1. The patient has not experienced clinical progression; and
2. Either:
    2.1. The patient has not experienced radiological progression; or
    2.2. The patient has experienced radiological progression but is not experiencing clinical progression and the treating clinician assesses the patient is still deriving clinical benefit.

11.5. In making this recommendation the Committee considered:

- Evidence of good treatment response rates in individuals
- The lack of long-term overall survival and quality of life data
- Many tumours are indolent for long periods of time, during this time belzutifan treatment may not improve health outcomes.

11.6. The Committee recommended Pharmac speak to international experts on the use of belzutifan with respect to the Special Authority criteria, when the most appropriate time to initiate treatment is, and if all individuals with renal cell carcinoma or pancreatic neuroendocrine tumours ≥3 cm will receive surgery.

11.7. The Committee recommended seeking advice from urologists if tumours ≤3 cm are treated with alternative surgical methods including cryoablation therapy.

Discussion

Māori impact

11.8. The Committee discussed the impact of funding belzutifan for the treatment of VHL on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee considered there was a sparsity of evidence on the prevalence of VHL in Māori. The Committee noted the Rare Disorders Advisory Committee discussed the impact of funding belzutifan for the treatment of VHL on Māori health outcomes in May 2024.

Populations with high health needs

11.9. The Committee discussed the health need(s) of individuals with VHL 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 belzutifan and considered that given the low prevalence of the disease, there was limited evidence to determine if there was a disproportionate effect on populations with high health needs. The Committee discussed the Rare Disorders Advisory Committee considerations of the impact of funding belzutifan for the treatment of VHL for populations with high health needs in May 2024.

Background

11.10. The Committee noted the Rare Disorders Advisory Committee (RDAC) recommended that CTAC review the application and recommend Special Authority criteria.

Health need

11.11. The Committee noted the considerations of the RDAC in May 2024 and patient lived experience provided to RDAC.

11.12. The Committee considered individuals with VHL had a high unmet health need, with the condition having a significant impact on their duration and quality of life.

11.13. The Committee considered the routine surveillance for individuals with VHL was intensive.

11.14. The Committee considered VHL affected individuals from a young age, with some individuals diagnosed before the age of 10, and the average age of diagnosis in people who were in their early thirties (Leeuwaarde et al. Gene Reviews. 2025, Wang et al. Transl Oncol. 2024;51:102193).

11.15. The Committee considered that renal cell carcinoma (RCC) and pancreatic neuroendocrine tumours (pNET) can be indolent and inactive for large periods of time.

11.16. The Committee considered that on average RCC is observed for two to four years before active management through surgery. The Committee noted approximately one third of tumours exhibit no growth over a median of 29 months. The Committee noted approximately 20% of renal tumours would be indolent and therefore potentially not require treatment (Jonasch et al. N Engl J Med 2021;385:2036-46, Leeuwaarde et al.2025, Wang et al. 2024).

11.17. The Committee considered for individuals with symptomatic central nervous system haemangioblastomas (CNS HB) the current treatment was surgery. The Committee considered this was associated with significant morbidity and mortality risk, particularly if the CNS HB were multifocal. The Committee noted 60% of CNS HB were asymptomatic, with the average surveillance before surgery of 33-38 months. The Committee noted approximately 80% of CNS HB would not be suitable for surgical treatment (Leeuwaarde et al.2025, Wang et al. 2024).

11.18. The Committee noted approximately 16% of pNETs required surgical intervention after an average of 23-53 months of surveillance (Leeuwaarde et al.2025, Wang et al. 2024).

11.19. The Committee considered current treatment options consisted of surgical interventions that were associated with a high risk of morbidity. The Committee considered that while the aim of surgery was to be organ preserving, increasing the time to surgery through slowing tumour growth would be beneficial to individuals with VHL.

11.20. The Committee considered individuals with VHL would not be managed with other anti-cancer therapeutics pre-operatively, and likely only be treated with a systemic anti-cancer therapy if there was progression post operatively.

Patient lived experience

11.21. The Committee noted in addition to the submissions received for the RDAC May 2024 meeting, it had received submissions from two patients living with VHL as well as a submission from the New Zealand Branch of the von Hippel-Lindau Family Alliance. The submissions described the patients' personal experience of living with

VHL and on their whānau, as well as their experiences of treatment within the New Zealand healthcare system.

11.22. The Committee wished to express their sincere gratitude to the individuals and patient group for their submissions and recognised the courage of sharing their personal stories and experiences.

Health benefit

11.23. The Committee noted the evidence and clinician feedback reviewed by the RDAC in May 2024.

11.24. The Committee noted the following updated health benefit evidence:

- Srinivasan et al. Lancet Oncol. 2025;26:571-82
- Else et al. Clin Cancer Res. 2024;30:1750-57.
- Iliopoulos Lancet Oncol. 2024;25:1325-36
- Wiley et al. Ophthalmology. 2024;131:1324-32

11.25. The Committee considered that individuals treated with belzutifan experienced a high response rate across the different tumour types.

11.26. The Committee considered belzutifan treatment was well tolerated. The Committee noted anaemia was the most common treatment related adverse event. The Committee considered this was commonly managed in clinical practice.

11.27. The Committee noted that 59% of individuals remained on treatment at three years.

11.28. The Committee considered it was reasonable to assume in symptomatic patients belzutifan treatment is likely to improve quality of life whilst on treatment.

Suitability

11.29. The Committee noted the considerations of the RDAC in May 2024.

Cost and savings

11.30. The Committee considered it was reasonable to assume there would be approximately 20 individuals with VHL in New Zealand who would be eligible for belzutifan treatment.

11.31. The Committee considered belzutifan treatment would not reduce the need for active surveillance, and therefore individuals would undertake the same number of clinic appointments and scans.

11.32. The Committee considered it was uncommon for individuals with small RCC tumours to require renal support in the form of dialysis, and therefore this should not be considered as part of the outcomes for economic modelling. The Committee considered a very small proportion (1 in 20) may end up with insufficient renal mass and require support. The Committee considered new surgical techniques were improving organ function preservation rates.

11.33. The Committee considered belzutifan treatment would delay time to expensive and potentially debilitating surgery, and the associated post operative support.

11.34. The Committee considered it may be reasonable to increase surveillance on tumours that are smaller than the surgical criteria that are showing progression to identify the appropriate time for belzutifan initiation. The Committee considered that this would reduce the overall population treated but would delay time to surgery as effectively.

Funding criteria

11.35. The Committee noted the proposed treatment paradigm was to initiate belzutifan treatment upon diagnosis of a tumour that did not require immediate surgical intervention. The Committee considered the time to progression to surgery for individuals under surveillance is variable and therefore it was challenging to define the optimal time for intervention with belzutifan.

11.36. The Committee considered it was not common to continue to treat, with the same treatment, tumours following radiological progression. The Committee considered further advice from an international expert may be appropriate to help define the Special Authority renewal criteria.

11.37. The Committee considered it may be more reasonable to consider initiating treatment based on a median change in tumour size over time for RCC tumours and pNETS, rather than to initiate treatment as soon as diagnosed. The Committee considered this would prevent unnecessary treatment, and side effects. The Committee considered this would prevent additional treatment in a large proportion of individuals with pNETS, with only 16% of pNETs requiring surgical intervention.

11.38. The Committee considered it would not be appropriate to apply a size criterion to CNS HB as these are resected based on symptoms and location, rather than size alone.

11.39. The Committee considered it was reasonable to restrict treatment to individuals who had not received prior systemic anti-cancer therapy. The Committee considered there was insufficient data to determine if those who had received a prior systemic anti-cancer therapy would derive the same benefit as those who had not.

11.40. The Committee considered it would be reasonable to seek international expert advice on if it would be appropriate to restrict treatment to individuals with growing tumours compared to all individuals with VHL associated tumours.

Summary for assessment

11.41. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for belzutifan if it were to be funded in New Zealand for VHL. 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.

11.42. The Committee noted that elements of the PICO (population, intervention, comparator, outcomes) for this application are uncertain at this time. The PICO may develop based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	People with VHL diagnosis, requiring treatment for either non-metastatic renal cell carcinoma with lesions ≤3 cm, central nervous system hemangioblastomas, or non-metastatic pancreatic neuroendocrine tumour not requiring immediate surgery, with an ECOG 0-2, and no prior systemic anti-cancer therapy.
Intervention	120 mg belzutifan, once daily (3 x 40-mg tablets) until clinical progression or intolerable toxicity. Belzutifan can be continued upon radiographic progression if the individual is not experiencing clinical progression and the treating clinician assesses the patient is still deriving clinical benefit.
Comparator(s)	Active surveillance based on the eviQ guidelines for VHL disease risk management (EviQ, ID 397 v.10, VHL disease-risk management).

Outcome(s)	The LITESPARK-004 (intervention) and VHL Natural History study (comparator) publications provide evidence of the benefit of belzutifan and inform transition probabilities for economic modelling. Key outcomes • Objective response rate • Duration of response • Progression-free survival • Delayed time to, or avoidance of surgery
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.	

12. Eltrombopag for aplastic anaemia, severe, 1st line, in combination with CSA and hATG immunosuppressive therapy (IST)

Application

12.1. The Committee reviewed the clinician application for widened access to eltrombopag (Revolade) for the first-line treatment of severe aplastic anaemia.

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

Recommendation

12.3. The Committee **recommended** that access to eltrombopag be widened to the first-line treatment of severe aplastic anaemia with a **high priority**, within the context of haematology treatments, subject to the following Special Authority criteria:

> **Initial application – (severe aplastic anaemia, first line).** Applications from any relevant practitioner. Approvals valid for 3 months for applications meeting the following criteria.
> All of the following:
> 1. Either:
> 1.1. Patient has severe or very severe aplastic anaemia with at least two of the following:
> 1.1.1. Absolute neutrophil count of less than 500 neutrophils per microlitre; or
> 1.1.2. Platelet count of less than 20,000 platelets per microlitre; or
> 1.1.3. Reticulocyte count of less than 60,000 reticulocytes per microlitre; or
> 1.2. Patient has severe aplastic anaemia with a platelet count of 20,000 to 30,000 platelets per microlitre and significant mucocutaneous bleeding; and
> 2. Disease is associated with a hypocellular bone marrow (<30% cellularity), without evidence of fibrosis or malignant cells; and
> 3. Eltrombopag to be used in combination with ciclosporin +/- antithymocyte globulin (ATG).
>
> **Renewal – (severe aplastic anaemia, first line).** Applications from any relevant practitioner. Approvals valid for 3 months for applications meeting the following criteria.
> 1. The patient has not received a response from treatment (at least 20,000 platelets per microlitre above baseline) during the initial approval period.

12.3.1. In making this recommendation, the Committee:

- Noted there is good quality evidence that in the first-line treatment of severe aplastic anaemia (AA), eltrombopag in combination with ciclosporin and horse

antithymocyte globulin (ATG) increases the rate of response and time to response from immunosuppressive therapy (IST), and decreases the requirement for red blood cell (RBC) and platelet transfusions than treatment with those two medicines alone

- Considered there is a strong clinical rationale for accessing effective treatment(s) early in the severe AA treatment paradigm to provide the greatest chance of response
- Considered that eltrombopag in combination with ciclosporin and horse ATG in the first-line treatment of severe AA would likely result in cost savings from reduced transfusion dependence.

12.4. The Committee **recommended** that access to eltrombopag be widened to the second-line treatment of relapsed/refractory severe aplastic anaemia with a **high priority**, within the context of haematology treatments, subject to Special Authority criteria.

12.4.1. In making this recommendation, the Committee:

- Considered that those whose severe AA has relapsed after, or is refractory to, IST including eltrombopag have the same health need as those requiring first-line IST with eltrombopag, noting some will relapse even with first-line IST with eltrombopag and are less likely to benefit from current second-line treatments
- Noted the lack of evidence for the response rate to eltrombopag in this second-line relapsed/refractory setting. However, the Committee again considered there is clinical rationale for using the most effective treatment combination at the next opportunity for severe AA to provide the greatest chance of response, which supported the concept of strengthening second-line IST with the addition of eltrombopag
- Considered that second-line eltrombopag with IST would provide the same benefit as first-line use in terms of transfusion dependence and may additionally provide savings by avoiding some long-term third-line use of eltrombopag.

12.5. The Committee considered it reasonable for the current eligibility criteria for eltrombopag to be amended to allow immediate access for people with severe AA with intolerance to other ISTs (relating to the criterion requiring a three-month trial of two other ISTs) or access for those with severe disease based on reticulocytopenia and neutropenia, with or without bleeding.

Discussion

Māori impact

12.6. The Committee discussed the impact of widening access to eltrombopag for the treatment of severe AA on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee noted that AA does not fall within the Hauora Arotahi (Pharmac Māori Health Areas of Focus). The Committee considered that there was no evidence to indicate that Māori are disproportionately affected by AA, however, acknowledged that inequities may exist in an absence of evidence.

Populations with high health needs

12.7. The Committee discussed the health need(s) of people with severe AA 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 widening access to eltrombopag and considered:

12.7.1. People with AA living rurally or at a distance from main treatment centres, or with poor access to transport are substantially impacted the disease due to distance from, and availability of, health services to promptly manage infections, provide treatment (usually at main centres) and administer transfusions (which may be required very frequently). Members specifically noted management of neutropenic fever in areas without 24-hour health care where antibiotics would be given after the individual is driven to the nearest hospital by ambulance or support person.

12.7.2. There was no evidence to indicate increased incidence or impact among other population groups.

Background

12.8. The Committee noted that eltrombopag is currently funded on the Pharmaceutical Schedule for severe aplastic anaemia (AA) after two immunosuppressive therapies (IST) have been used, and for people with idiopathic thrombocytopenic purpura (ITP) including idiopathic thrombocytopenic purpura contraindicated to splenectomy, subject to Special Authority criteria.

12.9. The Committee noted that eltrombopag has been funded for some individuals (about two to four people per year) with severe AA through the Named Patient Pharmaceutical Assessment (NPPA) pathway. The individuals whose funding has been approved through the NPPA pathway is defined as “those who have transfusion dependent disease and have either not tolerated or responded to immunosuppressive therapy; or those whose disease trajectory is sufficiently rapid/severe that a response to immunosuppressive therapy has not been able to be determined.”

Health need

12.10. The Committee noted that AA is an acquired immune-mediated disease of bone marrow failure with very high mortality (>80%) if left untreated (Williams et al. Blood. Clin Haematol. 1978;7:467-74). The Committee noted that diagnosis of AA requires two of the following cytopenias: thrombocytopenia (platelets <20,000 per microlitre), neutropenia and/or reticulocytopenia (reticulocytes <60,000 per microlitre), and a hypocellular bone marrow on biopsy. The Committee noted that severe AA and very severe AA can be defined as having an absolute neutrophil count of either <500 per microlitre (severe) or <200 per microlitre (very severe) (Camitta et al. Lancet. 1988; 331:303-4).

12.11. Members considered a neutrophil count of <500 per microlitre is highly important due to the serious risk of infection and potential for overwhelming bacterial sepsis, and platelets of <10,000 per microlitre can be associated with spontaneous bleeding, requiring hospital admissions and red blood cell (RBC) and/or platelet transfusions. Members considered that for an individual with severe AA, a fever requires hospital admission for appropriate management and an inpatient stay often lasts three to five days. The Committee noted that in AA, haematopoietic stem cells can develop accumulating somatic mutations, and the disease comes with a risk of clonal evolution to acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS).

12.12. The Committee noted the significance of the bimodal age peak for AA incidence (as reported by Vaht et al. Haematologica. 2017;102:1683-90), given that younger patients are more likely to be candidates for potentially curative treatment with a stem cell transplant (SCT) instead of first-line immunosuppressive therapy (IST) consisting of cyclosporin (CSA) +/- horse antithymocyte globulin (ATG). Members considered

that IST can be associated with serum sickness and that older patients and/or those with comorbidities may not be suitable for ATG and therefore may receive ciclosporin alone for IST.

12.13. Members considered there is increasing use of SCT with alternative, non-sibling donors although the capacity for SCT in New Zealand was an impactful factor. The Committee noted that SCT is the preferred first-line treatment based on greater disease-free survival and a lower risk of clonal evolution with SCT compared with IST (Scheinberg et al. Blood Adv. 2026 Mar 24:bloodadvances.2025019051), however, SCT is associated with a higher risk of mortality and graft-versus-host disease.

12.14. The Committee noted the estimated number of patients who might receive eltrombopag within first-line therapy suggested by the applicant (6 to 10 per year) and by Pharmac staff (slightly higher based on Special Authority data indicating approximately eight per year receiving eltrombopag second line; range: 3 to 12). The Committee noted that approximately 80% of patients in the Swedish registry study were reported to receive first-line IST and considered it reasonable to estimate that approximately 15 people per year might receive first-line IST in New Zealand, based on this proportion and an incidence of 3 per million in the population (Vaht et al. Haematologica. 2017;102:1683-90).

12.15. The Committee considered AA has a substantial impact on an individual's quality of life (QOL) from bleeding risk, chronic anaemia, transfusions which may be required frequently (eg weekly) and recurrent hospital admissions. The Committee acknowledged the impact of AA on family and whanau who help manage frequent transfusions, transport and support.

12.16. The Committee considered the current impact to the health system for managing AA includes costs associated with chair time to manage blood transfusions. The Committee considered most transfusions require two units totalling six hours of infusion time plus intravenous access time, and a substantial amount of chair time is needed for regular transfusions occurring once or twice a week for patients with severe AA.

12.17. The Committee considered that those whose severe AA has relapsed after, or is refractory to, IST including eltrombopag have the same health need as those requiring first-line IST with eltrombopag, noting some will relapse even with first-line IST with eltrombopag and are less likely to benefit from current second-line treatments. Members considered that ~20% of individuals with severe AA would have disease refractory to ATG and ~30% refractory to CSA. Of these, younger individuals might subsequently be candidates for SCT and those who are older might be offered treatment with rabbit ATG. Members considered there is clinical rationale for using the most effective treatment combination at the next opportunity for severe AA to provide the greatest chance of response.

Health benefit

12.18. The Committee noted that eltrombopag is an oral treatment which stimulates stem cell proliferation, has immunomodulatory effects, and is associated with a time-to-response of about three-months in severe AA.

12.19. The Committee noted that eltrombopag is recommended by the following guidelines:

12.19.1. American Society of Hematology (ASH) 2026 Guidelines: Added to IST for severe AA/very severe AA (conditional recommendation, based on low certainty of the evidence of the effects; Scheinberg et al. Blood Adv. 2026:bloodadvances.2025019051)

12.19.1.1. British Society for Haematology (BSH) Guideline 2024: Recommends (pending regulatory approval) horse ATG with CSA and eltrombopag for

severe AA/very severe AA instead of current standard first-line IST with horse ATG and CSA (grade 1B; Kulasekararaj et al. Br J Haematol. 2024;204:784–804).

12.19.1.2. American Society for Transplantation and Cellular Therapy (ASTCT) Guidelines: recommend eltrombopag be added to IST for individuals not suitable for transplant (Iftikhar et al. Transplant Cell Ther. 2024;30:1155-70).

12.20. The Committee noted the CETB11 5AUS single centre, single arm, open-label sequential cohort study which included 92 patients with severe aplastic anaemia who had not received prior definitive IST (Townsley et al. N Engl J Med. 2017;376:1540-50). Participants across three cohorts received IST (ATG and CSA) plus eltrombopag for either three or six months.

12.20.1. The Committee noted that after median follow-up of 23 months, the rates of complete (CR) and partial (PR) haematologic responses in all cohorts were 30% and 50%, respectively, at three months and 39% and 48%, respectively, at six months. The time to haematologic response was improved for neutrophil and platelet counts with eltrombopag plus IST compared with historical controls who received IST.

12.20.2. The Committee noted the study had long follow-up of five years, and that four-year overall survival (OS) rates were 92.5% and 85% in the eltrombopag plus IST and IST groups, respectively. The Committee noted that most deaths were due to infection with concurrent neutropenia and that survival was the same for those who received either a PR or CR.

12.21. The Committee noted the phase III EBMT-Saawp RACE Trial which investigated first-line ATG and CSA without (Group A) or with (Group B) eltrombopag in 197 people with severe AA/very severe AA (Peffault de Latour. N Engl J Med. 2022;386:11-23;). Eltrombopag 150 mg/d was given until six months, or three months in cases of early complete response.

12.21.1. The Committee noted the trial definitions of response and members considered that a PR was a good response in the context of severe AA with impacts on bleeding and infection risk, and an expected reduction in transfusion burden.

12.21.2. The Committee noted that after median follow up of 24 months, the primary outcome of CR rate at three months was 10% for Group A compared with 22% for Group B (pooled odds ratio, 3.2; 95% CI, 1.3 to 7.8; p=0.01). The overall response rate at six months was 41% for Group A compared with 68% for Group B, and the median time to response was 8.8 months for Group A compared with 3.0 months for Group B.

12.21.3. The Committee noted that, among responders, the time to platelet transfusion independence was 68 days in Group A and 40 days in Group B and the time to RBC transfusion independence was 140 days in Group A and 51 days in Group B. Members considered these differences reflected a significant improvement in this context and that the reported differences between groups for first response and complete response were also measures relevant to the transfusion burden associated with severe AA.

12.21.4. The Committee noted that there was no evidence of improved OS with eltrombopag at two years although the trial provided insufficient follow-up for this outcome and members considered there appeared to be a trend for improved OS.

12.21.5. The Committee noted that the two-year event-free survival in Group A was 32.7% compared with 48.4% in Group B, and disease-free survival was 36.6% and 54.7%, respectively (Risitano et al. Blood. 2024; 144:302(Suppl 1). The Committee considered that these differences would be expected to reduce the need for second-line treatments although the trial was underpowered for detecting a meaningful change in subsequent SCT rates with eltrombopag.

12.21.6. The Committee noted that toxicity was minimal and similar between groups. The Committee considered that while no reduction in infections was reported, this could reasonably be inferred from neutrophil counts increasing above 500 per microlitre.

12.22. The Committee noted that quality of life (QOL) scores in the EBMT-Saawp RACE Trial improved from baseline over time, and that QOL in the CETB11 5AUS trial was higher in those responding to treatment. Members considered this QOL improvement was associated with a reduced need to seek medical attention for bleeding or infection episodes and improved fatigue from a reduction in anaemia.

12.23. The Committee considered the evidence generalisable and very relevant to the New Zealand context, indicating very clinically significant benefits namely the reduction in life threatening cytopenias and transfusion burden. The Committee considered that further evidence was unlikely to eventuate as this is now standard of care in many countries.

12.24. The Committee noted the lack of evidence for the response rate to eltrombopag in the second line setting for relapsed or refractory severe AA. However, the Committee again considered there is clinical rationale for using the most effective treatment combination at the next opportunity for severe AA to provide the greatest chance of response, which supported the concept of strengthening second-line IST with the addition of eltrombopag. Members considered that second-line eltrombopag with IST would be expected to provide the same benefit as in the first-line, specifically in terms of transfusion dependence and may additionally avoid some third-line use of eltrombopag. Members considered that accessing eltrombopag again for the treatment of disease that has relapsed within 12 months would be reasonable and that this may reduce the number of patients requiring long courses of eltrombopag monotherapy in the third line.

Cost and savings

12.25. The Committee considered that if eltrombopag were funded in the first line setting for severe AA/very severe AA it would be unlikely to increase the total population treated and would not be expected to reduce the number of people proceeding for a first-line SCT.

12.26. The Committee considered that for most clinicians would prefer to offer the combination of all three therapies (hATG, CSA and eltrombopag) first-line if an individual was fit to receive them all but was not a candidate for SCT. However, members considered there is evidence to support CSA and eltrombopag in patients for whom ATG is not suitable (SOAR trial; Scheinberg et al. Lancet Haematol. 2024;11:e206-15).

12.27. The Committee considered that eltrombopag would not be used as monotherapy in the first line setting given the need for other treatments to make the necessary impact on the disease, noting this is not recommended by clinical guidelines, and given the risks associated with first-line eltrombopag monotherapy due to its stimulating effect on stem cells and potential clonal evolution.

12.28. The Committee considered that the duration of treatment would be up to six months, noting that the proportions stopping treatment due to CR in the RACE trial were 22% at three months and 32% by six months.

Funding criteria

12.29. The Committee noted that the evidence was for up to six months' treatment in the first line setting, with the RACE trial treatment stopped after three months where patients received a response. The Committee considered it reasonable to have an initial approval of three months with potential for a renewal for three months if response was yet to be received.

12.30. The Committee considered it reasonable to include a requirement for eltrombopag to be used in combination with IST (CSA and horse ATG or in combination with CSA alone for those not fit for ATG) in the first line setting to align with the evidence and clinical guidelines.

12.31. The Committee noted the current eligibility criteria for eltrombopag do not allow immediate access for people with severe AA with intolerance to other ISTs (relating to the criterion requiring a three-month trial of two other ISTs) or access for those with severe disease based on reticulocytopenia and neutropenia, without severe thrombocytopenia. The Committee considered it reasonable to amend the current eligibility criteria for eltrombopag to enable access for these situations which are estimated to include two to four individuals per year.

Summary for assessment

12.32. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for eltrombopag if it were to be funded in New Zealand for first-line treatment of severe AA. 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	Patients with severe or very severe aplastic anaemia who are not candidates for first line HLA matched sibling allogeneic stem cell transplant (SCT)
Intervention	Eltrombopag, first line treatment for up to 6 months (application suggests review at 3 months and discontinuation if response has been achieved) Eltrombopag is taken in combination with cyclosporin (CSA) +/- horse ATG (hATG) where these are appropriate and tolerated.
Comparator(s)	Current first line treatment is immunosuppressive therapy (IST) with CSA and hATG Eltrombopag may be considered second line after failure of first line IST

Outcome(s)	• Complete response • Haematologic (overall) response • Time to response • Quality of life • Overall survival (potentially) • Adverse events • Value of transfusion independence Evidence suggests no meaningful change in subsequent SCT rates with eltrombopag, with 12 and 11 HSCT received in each arm of the EBMT-Saawp RACE Trial (Peffault de Latour, R. N Engl J Med 2022;386:11-23).
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.	