Record of the Cancer Treatments Advisory Committee Meeting held on 20 November 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
Alice Minhinnick
Allanah Kilfoyle
Chris Frampton
Lochie Teague
Matthew Strother
Oliver Brake
Richard Isaacs
Scott Babington
Vidya Mathavan

Apologies
Michelle Wilson

2. Summary of recommendations

	Pharmaceutical and Indication	Recommendation
6.6	Pembrolizumab for the treatment of metastatic, MMR deficient stage 4, pancreatic adenocarcinoma	Decline
6.12	Cabozantinib for the second line treatment of advanced clear cell renal cancer	Decline
6.13	Everolimus for HR+, HER2- advanced breast cancer	Decline
6.14	Ipilimumab in combination with nivolumab for the first line treatment metastatic kidney cancer with a clear cell component, in individuals with poor, intermediate and favourable IMDC risk prognoses	Decline
6.15	Bevacizumab for the neoadjuvant treatment of metastatic colorectal cancer (mCRC) confined to the liver	Decline
8.3	Olaparib for the treatment of HER2 negative metastatic breast cancer with a germline *BRCA* mutation, subject to Special Authority criteria	Low Priority
8.5	Olaparib for the treatment of HER2 negative metastatic breast cancer with a *PALB2* mutation	Decline
9.3	Olaparib for the treatment of early high risk *BRCA*m HER2 negative breast cancer after neoadjuvant or adjuvant chemotherapy, subject to Special Authority criteria	High Priority

10.3	Abemaciclib for the adjuvant treatment of HR positive, HER2 negative early breast cancer, subject to Special Authority criteria	High Priority
10.4	Ribociclib for the adjuvant treatment of HR positive, HER2 negative early breast cancer, subject to Special Authority criteria	Medium Priority
11.3	Belantamab mafodotin for the treatment of relapsed or refractory multiple myeloma (2nd line or later), subject to Special Authority criteria	High Priority
12.3	Nivolumab for the treatment of resectable non-small cell lung cancer, subject to Special Authority criteria	High Priority

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'.

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.

5.5. The Committee noted the following updates to the medical devices programme:

5.5.1. The Cabinet's decision for a new approach in relation to the evaluation and procurement of hospital medical devices, as set out in the Minister's Joint Letter of Expectations (LoE) to Health NZ and Pharmac.

5.5.2. Pharmac and Health NZ have agreed on dividing medical device categories that are most focused on their particular capabilities and expertise and acknowledged that more information about the categories for Pharmac are on the website.

5.5.3. Pharmac is working with Health NZ to implement the joint operational approach and further information will be shared when it is available.

6. Cancer application priority and planning discussion

Committee planning discussion

6.1. Pharmac shared that it was actively recruiting for new Committee members and looking to expand membership numbers to build capacity and share the workload. The Committee was supportive of the Committee membership providing geographical balance across regions, to ensure input from larger and smaller cancer centres, as well as urban and rural populations. The Committee supported the recruitment of an expert from a centre providing allogenic transplants to support on consideration of the relevant haematological malignancy applications.

6.2. The Committee was supportive of a range of different meeting formats to ensure a higher volume of applications could be reviewed, this included online and in person, as well as full or half day meetings.

6.3. Pharmac staff sought the Committee's advice on the planning, prioritisation and rationalisation of the large volume of cancer treatment applications currently awaiting clinical advice or assessment.

6.4. Pharmac staff further sought advice on the next best steps for applications that had previously received clinical advice.

Applications previously deferred

6.5. The Committee discussed six applications which have previously received a defer recommendation from CTAC or PTAC.

6.6. The Committee noted that pembrolizumab for the treatment of metastatic, MMR deficient stage 4, pancreatic adenocarcinoma was deferred by CTAC in July 2023. The Committee **recommended** pembrolizumab for the treatment of metastatic, MMR deficient stage 4, pancreatic adenocarcinoma be **declined**. The Committee considered that the available evidence indicated an uncertain and likely small magnitude of benefit, based on subgroup analysis of a single-arm trial. The Committee considered it was unlikely further high-quality evidence of health benefit would become available, however would welcome further evidence if it does The Committee considered that the

patient population size was likely small and the evidence base did not support an assessment of pembrolizumab in this setting.

6.7. The Committee noted that pertuzumab with trastuzumab (PHESGO) for the adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence had previously been deferred by PTAC in 2022. Members noted that consultation feedback had highlighted updated evidence indicating a survival benefit with pertuzumab and trastuzumab compared with trastuzumab alone. The Committee considered that it was appropriate, given the updated evidence, for the Committee to formally review this at a future meeting before making a recommendation. The Committee considered however that the evidence indicated a relatively modest benefit for pertuzumab.

6.8. The Committee noted the application for cemiplimab for the treatment of metastatic or locally advanced cutaneous squamous cell carcinoma, not eligible for curative surgery or radiation that was deferred by CTAC in November 2021. The Committee considered new evidence was required to support the application. The Committee were made aware of a change in supplier for this product that may provide additional evidence. The Committee considered it wished to review the new evidence alongside the previous evidence at a future meeting.

6.9. The Committee considered osimertinib for the adjuvant treatment of EGFR mutated non-small cell lung carcinoma after tumour resection, that was deferred by CTAC in July 2023. The Committee considered it should be re-reviewed with updated overall survival data from the supplier. The Committee considered that if no further data is provided, it would be appropriate to close the proposal, given that the previously reviewed evidence did not support a positive funding recommendation.

6.10. The Committee noted the application for hexylaminolevulinate hydrochloride for the diagnostic detection of bladder cancer under blue, fluorescent light was deferred by (then) CaTSoP in 2018. The Committee considered that there was uncertainty about whether there remained a clinical need for this product, and that there had likely been technological developments in this therapeutic area that may supersede this proposal. The Committee suggested Pharmac staff reach out to the Urology Society to understand the benefit of this technology, and the current clinical need.

6.11. The Committee noted that there were currently two open proposals for pembrolizumab for the treatment of first line persistent, recurrent or metastatic cervical cancer with a PD-L1 combined positive score of 1 or more. The Committee noted that the proposal for the funding of pembrolizumab with bevacizumab received a decline recommendation by PTAC in May 2024, and that at the same meeting, PTAC had recommended the funding of pembrolizumab (with or without concomitant bevacizumab) with a high priority. The Committee considered having both proposals open was likely to result in confusion, and that it was appropriate to close the application that was declined by PTAC and retain the proposal that was agnostic to concomitant bevacizumab use, given that this was more reflective of the available data.

Other applications – seeking next steps

6.12. The Committee considered cabozantinib for the second line treatment of advanced clear cell renal cancer has been superseded by recent funding decisions. The Committee considered there was no significant clinical need in this treatment space. The Committee **recommended** this application be **declined**, with the option to reconsider the application should there be a commercial need in the future.

6.13. The Committee noted the application for everolimus for HR+, HER2- advanced breast cancer, and noted that this had previously been recommended for decline by PTAC in

2019. The Committee noted that consultation feedback on a proposal to decline this application had provided additional information on the benefit of everolimus. The Committee considered that the additional information provided was not sufficient to change PTAC's previous decline recommendation and **recommended** that the application for everolimus be **declined**. The Committee considered there was a range of other treatment options in this setting with a less toxic side effect profile.

6.14. The Committee noted the application for ipilimumab in combination with nivolumab for the first line treatment of metastatic kidney cancer with a clear cell component, in individuals with poor, intermediate and favourable IMDC risk prognoses, was recommended with a low priority by CTAC in July 2023. The Committee **recommended** the application which includes the favourable risk group be **declined** given recent funding for individuals in the poor/intermediate risk group. The Committee noted that the evidence previously reviewed by the Committee indicated little benefit for those with a favourable risk score, based on post-hoc trial evidence.

6.15. The Committee noted the application for bevacizumab for the neoadjuvant treatment of metastatic colorectal cancer (mCRC) confined to the liver was deferred by CTAC in April 2025, noting it was unclear where bevacizumab might provide the greatest benefit in mCRC. The Committee **recommended** bevacizumab for the neoadjuvant treatment of metastatic colorectal cancer confined to the liver be **declined** following clinical input from the Gastrointestinal Cancers Special Interest Group (GISIG). The Committee noted the GISIG indicated there was not a strong desire for bevacizumab as a 'downstaging' treatment (as described for the existing proposal).

6.16. The Committee considered early clinical feedback from the GISIG would provide valuable input into the best pathway and clinical need for applications.

Applications that have not received clinical advice

Pharmac staff sought advice on how best to prioritise applications that have been accepted and await clinical advice. Members reviewed the current list of applications and provided feedback to Pharmac staff to collate. This will inform a CTAC workplan for 2026 which will be further developed with ongoing input from members.

6.17. Members considered relevant health need, strength and quality of evidence, and availability of alternatives within their priorities.

6.18. The Committee noted that Pharmac staff will also engage with other relevant clinical groups (including SIGs) to seek their views.

6.19. The Committee noted that within the setting of lung cancer applications, it would prioritise applications with overall survival data, for example consolidation durvalumab for limited small cell cancer, whilst others such as adjuvant alectinib had data that was currently limited to progression free survival benefit.

6.20. The Committee considered some of the applications could be reviewed by the Haematology Advisory Committee.

7. Matters Arising – Rule 8.1b and AYA patient group discussion

Discussion

Background

7.1. The Committee noted that Pharmac had previously undertaken a substantive review of Rule 8.1b which currently provides access to medicines for children with cancer in a paediatric setting.

7.2. The Committee noted that, as part of this review, Pharmac committed to considering whether action could be taken within existing budget to address inequities in access to

cancer medicines for adolescents and young adults (AYA) with paediatric-origin cancers who are treated in adult services.

7.3. The Committee noted that Pharmac staff had engaged with the AYA Cancer Network, paediatric oncology services, and clinical leads to inform the development of options to address these inequities.

General

7.4. The Committee noted that Rule 8.1b currently provides funded access to medicines without a full Pharmac assessment when patients are treated in a paediatric oncology setting, irrespective of age, and that most children and young people with paediatric-origin cancers already benefit from this provision.

7.5. The Committee noted that nationally AYA is generally defined as ages 12–24. However, 12–14-year-olds are treated exclusively in paediatric settings and therefore already have access to medicines under Rule 8.1b. This discussion focuses on AYAs aged 15 to 24 years who may be treated in adult services and therefore do not currently benefit from the funding rule.

7.6. The Committee noted evidence indicating poorer survival outcomes for AYA with cancer compared with children receiving similar treatments, and that inequities in access to medicines were considered one contributing factor.

7.7. The Committee noted that retaining the status quo, with improved monitoring and data collection but no extension of access under Rule 8.1B, would not address the identified inequities in access and health outcomes for AYA.

7.8. The Committee noted that while an age-based extension could address some of these challenges, it would introduce a hard age cut-off and create a new eligibility cliff, with ongoing concerns about fairness for those just outside the defined age range.

7.9. The Committee noted that tumour biology-based access aligned with clinical understanding that treatment effectiveness and expected outcomes are largely driven by the biological characteristics of the cancer rather than chronological age of the person.

7.10. The Committee discussed concerns that a tumour biology-based approach could increase fiscal risk if eligibility were perceived as extending more broadly into adult populations, particularly for cancers such as acute lymphoblastic leukaemia where effective therapies are increasingly available for adults who could potentially be treated under a similar regime to children and AYA groups.

7.11. The Committee noted concerns that some newer medicines, including bispecific antibodies, may be used outside formal paediatric protocols and could be beneficial and well-tolerated in older adults, making it more difficult to limit access in practice.

7.12. The Committee discussed whether linking eligibility to treatment on a paediatric-based protocol could provide a mechanism to manage scope and risk, while acknowledging that protocols evolve over time and not all medicines are used strictly within formal protocols.

7.13. The Committee noted the importance of understanding the epidemiology of paediatric-origin cancers across age groups in New Zealand, and that further work to map diagnoses, age distribution, and likely medicine use would help clarify the fiscal implications of any extension.

7.14. The Committee discussed human rights and equity considerations, noting that the review of Rule 8.1b originated in part from concerns about inequitable access to funded medicines for children with conditions other than cancer. Members noted that extending access to AYA may reduce inequity for that group, while also raising questions about consistency with access for other non-cancer conditions.

7.15. The Committee considered a need for greater support for approaches that avoid strict age-based cut-offs and better reflect tumour biology and clinical practice, while recognising the need for safeguards to manage scope and cost.

7.16. The Committee considered that any proposal to extend Rule 8.1b would benefit from further refinement, including clearer definitions, consideration of protocol-based access, and additional data on potential patient numbers and fiscal impact.

8. Olaparib for the treatment of HER2 negative metastatic breast cancer with either a *BRCA* or *PALB2* mutation

Application

8.1. The Committee reviewed the application for olaparib for the treatment of human epidermal growth factor receptor 2 negative (HER2-) metastatic breast cancer with either a BReast CAncer (*BRCA*) or Partner and Localiser of BRCA2 (*PALB2*) mutation

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 olaparib for the treatment of HER2 negative metastatic breast cancer with a germline *BRCA* mutation be funded with a **low priority**, within the context of treatment of malignancy, subject to the following Special Authority criteria:

> **Initial application – (breast cancer, metastatic)** only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1. Either
>   - 1.1. Patient has recurrent or de novo metastatic triple negative breast cancer (that does not express ER, PR or HER2 ICH3+, or ISH+ [including FISH or other technology]); or
>   - 1.2. Patient has recurrent or de novo unresectable, inoperable locally advanced or recurrent or de novo metastatic cancer that is confirmed as hormone receptor positive and HER2-negative; and
> 2. Patient has breast cancer that has a class 4 or 5 *BRCA1* or *BRCA2* gene mutation; and
> 3. Either:
>   - 3.1. Patient has received systemic (neo)adjuvant chemotherapy; or
>   - 3.2. Patient must have been diagnosed with de novo metastatic disease and received chemotherapy in the metastatic setting; and
> 4. Patients with hormone-receptor positive breast cancer must have received at least one line of endocrine therapy (either in the adjuvant or the metastatic setting) and had disease progression during therapy, unless they had disease for which endocrine therapy was considered inappropriate; and
> 5. Olaparib to be discontinued at disease progression; and
> 6. Total treatment with olaparib must not exceed two years.
>
> **Renewal application – (breast cancer, metastatic)** only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1. No evidence of disease progression; and
> 2. Olaparib to be discontinued at disease progression; and
> 3. Total treatment with olaparib not to exceed two years

8.4. In making this recommendation the Committee considered:

- The high health need of individuals with *BRCA* mutated HER2 negative metastatic breast cancer
- The lower efficacy of funded treatments for individuals with *BRCA* mutations

- The evidence of progression free survival (PFS) but no overall survival (OS) benefit
- The need for expanding *BRCA* testing nationwide to ensure equitable access.

8.5. The Committee **recommended** that olaparib for the treatment of HER2 negative metastatic breast cancer with a *PALB2* mutation be **declined**.

8.6. In making this recommendation the Committee considered:

- The high health need of individuals with *PALB2* mutated HER2 negative metastatic breast cancer
- The lack of evidence of health benefit in individuals with *PALB2* mutations.

Discussion

Māori impact

8.7. The Committee discussed the impact of funding olaparib for the treatment of HER2 negative (HER2-) metastatic breast cancer with either a *BRCA* or *PALB2* mutation on Māori health areas of focus | Hauora Arotahi and Māori health outcomes.

8.7.1. The Committee noted the treatment of breast cancer is a Hauora Arotahi (Pharmac Māori Health Areas of Focus).

8.7.2. The Committee noted the Lattimore study that screened 367 individuals with breast cancer to identify *BRCA/PALB2* mutation status in New Zealand identified that of the individuals who specified their ethnicity, 7.1% (23/322) identified as Māori or as having Māori ancestry. On average, Māori were found to be slightly younger at diagnosis compared to non-Māori (57.6 vs 63.1 years), and a higher proportion were diagnosed with grade 3 tumours compared to non-Māori (60.9% vs 47.8%), but these clinical differences did not reach statistical significance (Lattimore et al Breast Cancer Res Treat. 2021;185:583-90).

8.7.3. The Committee considered that as reference databases were predominantly compromised of individuals from European descent it was more likely Māori would have variants of unknown significance which would impact the diagnostic accuracy of testing.

Populations with high health needs

8.8. The Committee discussed the health need(s) of HER2- metastatic breast cancer with either a *BRCA* or *PALB2* mutation 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 olaparib and considered:

8.8.1. As reference databases were predominantly compromised of individuals from European descent it was more likely Māori and Pacific peoples would have variants of unknown significance which would impact the diagnostic accuracy of testing.

8.8.2. The current pilot program for *BRCA* and *PALB2* testing is limited to major cancer centres, therefore there is an inequity in the diagnostic availability across New Zealand, especially for individuals in rural areas or located a greater distance from major cancer centres.

Background

8.9. The Committee noted that ribociclib and palbociclib are funded for the treatment of locally advanced/metastatic, HER2-, hormone receptor positive (HR+) breast cancer. The Committee noted these are cyclin-dependent kinases 4 and 6 inhibitors (CDK4/6i).

8.10. The Committee noted olaparib is funded for the second line treatment of high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer in individuals with a germline *BRCA1* or *2* gene mutation. The Committee noted olaparib is a Poly (ADP-ribose) polymerase (PARP) inhibitor.

Health need

8.11. The Committee noted the health need of individuals with metastatic triple negative breast cancer (TNBC) were recently discussed in October 2023 and therefore focused on the specific health need of individuals with a *BRCA* or *PALB2* pathogenic variant.

8.12. The Committee considered there were changes in the classification of HER2 expression, with many HER2- tumours now being classed as HER2 low and ultralow. The Committee considered that as well as altering the treatment paradigm, it would also affect the proportion of individuals who were categorised as TNBC, and consequently the population size.

8.13. The Committee noted a large French retrospective database study with HR+ HER- metastatic breast cancer (Frenel et al. Br J Cancer. 2023;128:2072-80). The Committee noted approximately 3% were tested for germline *BRCA* mutations (*BRCA*m*)*, with approximately 170 people identified as having a *BRCA*m. The Committee noted individuals with a *BRCA*m who are HR+ had a poorer progression free survival and overall survival when treated with first line endocrine therapy compared to wildtype.

8.14. The Committee considered similar results were reported by a retrospective cohort study when treated with a first line CDK4/6i. Therefore, the Committee considered individuals with a *BRCA*m had a poorer outcome and reduced efficacy from currently funded therapies. The Committee considered therefore this would have a negative effect on the individual and their whānau caring for them.

BRCA

8.15. The Committee noted *BRCA*m carriers have an approximately 70% cumulative risk of developing breast cancer by 80 years of age (Arun et al. Br J Cancer; 2024: 131, 1400–414). The Committee noted *BRCA*m are detected in ~5% of unselected people with breast cancer and in ~25% with a family history of breast or ovarian cancer.(Armstrong et al. Clin Epidemiol. 2019;11:543–61). Individuals with a *BRCA1*m are predisposed to TNBC whereas people with a *BRCA2*m most often have ER+ tumours (Antoniou et al. *Breast Cancer Res* 2012;14:R33-R33)(Mavaddat et al. *Cancer Epidemiol Biomarkers Prev* 2012;21:134-47).

8.16. The Committee considered the effect of *BRCA*m carrier status on prognosis and outcomes is unclear, with additional studies required.

PALB2

8.17. The Committee noted studies of familial breast cancer have yielded estimates of risk in association with loss-of-function mutations in *PALB2* that are two to four times as high as the risk among non–mutation carriers (Antoniou et al. N Engl J Med 2014;371:497-506). The eviQ guidelines report an average breast cancer risk of 53% by 80 years of age for *PALB2*m carriers compared to a population risk of 11.9%.

8.18. The Committee noted estimates that 0.6%–3% of patients with breast cancer have a likely disease-causing mutation or disease-causing mutation in *PALB2* (Casadei et al. Cancer Res. 2011;71:2222-9) and approximately 1.2% of patients with TNBC carry such a mutation (Couch et al. J Clin Oncol. 2014 Dec 1;33:304–11). A study also reported patients with TNBC with mutations were diagnosed at an earlier age ($P <$ .001) and had higher-grade tumours ($P = .01$) than those without mutations (Couch et al. 2014).

Screening

8.19. The Committee noted the 2022 Te Rēhita Mate Ūtaetae report published by NZBCF found that 5% of patients with breast cancer diagnosed since 2013 were tested for *BRCA*, and of these 14% had g*BRCA1*m, 10% had *BRCA*2m, and 76% had no mutation detected.

8.20. The Committee considered guidelines recommend the screening of individuals at higher risk however noted a 2021 study (Ciuro et al. Clin Breast Cancer. 2021;21:e220-e227) suggested guidelines needed to be revised and further studies are required to identify high risk populations, health care disparities, and socioeconomic barriers to genetic testing.

8.21. The Committee considered pathogenic variants, and their clinical outcomes may not have been fully delineated in the New Zealand population, with reference data bases comprised of individuals mainly from European descent. Therefore, the Committee considered it was more likely Māori and Pacific peoples would have variants of unknown significance. The Committee considered there was evidence that variants that are considered non-pathogenic in European descent populations are pathogenic in other populations.

8.22. The Committee noted both *BRCA* and *PALB2* mutations can arise as a germline or somatic mutation. The Committee noted that only germline testing was performed as standard in New Zealand.

8.23. The Committee considered that current screening for *BRCA* mutations have been driven by the BOADICEA algorithm. The Committee considered this provided a risk estimate of carrying a *BRCA* pathogenic variant. The Committee noted the risk threshold for access to testing has decreased from 20 to 10%.

8.24. The Committee noted a New Zealand study that screened a cohort of 367 people with breast cancer reported that 13 (3.5%) carried a mutation that causes breast cancer or a mutation that is likely to cause breast cancer in *BRCA1, BRCA2, PALB2*, or *PTEN*. A significantly higher number of mutation carriers had grade 3 tumours (10/13) when compared to non-carriers. In the cohort, 46% of the identified (likely) mutation carriers had not been referred for a genetic assessment and consideration of genetic testing (Lattimore et al Breast Cancer Res Treat. 2021;185:583-90). The Committee noted a UK study reported up to 50% of individuals with a *BRCA* pathogenic variant were not identified. The Committee considered a similar proportion were likely not identified in New Zealand.

8.25. The Committee were informed of a new Pilot Mainstreaming Program for germline mutational testing of breast cancers. The Committee noted, that to be enrolled, the individuals had to be domiciled to the pilot regions and not had previous genetic testing. The Committee noted the testing also extended the gene panel to include *BRCA1/2, CHK2, ATM, PALB2, CDH1,* and *RAD51 C& D*.

8.26. The Committee considered the pilot program will increase testing in some regions but with a likely bias to testing those with newly diagnosed breast cancer. The Committee considered therefore the screening was likely only accessible to individuals near major cancer centres, and there was likely to be a prevalent population that are not included in the testing.

8.27. The Committee considered in New Zealand there was currently no system to review variants of unknown significance that have been identified and reclassify them in the future based on new pathological variants identified in the reference databases.

Health benefit

Germline *BRCA* mutations

8.28. The Committee noted OlympiaD, a randomised, controlled, open-label, multicentre, international, phase three trial (N=302) that compared olaparib to physician choice of chemotherapy (TPC).

8.28.1. The Committee noted Robson et al. Eur J Cancer. 2023:184:39-47 that reported data at 76.8% maturity:

- The median overall survival (OS) was 19.3 months for olaparib vs 17.1 months for TPC (hazard ratio (HR) 0.89, 95% confidence interval (CI) 0.67-1.18); median follow-up was 18.9 and 15.5 months, respectively.
- Three-year survival was 27.9% for olaparib vs 21.2% for TPC.
- In first-line, median OS was longer for olaparib than TPC (22.6 vs 14.7 months; HR 0.55, 95% CI 0.33-0.95).

8.28.2. The Committee noted Robson et al. Ann Oncol.2019;30:558–66 that reported data at 64% maturity.

8.28.3. The Committee noted Robson et al. N Engl J Med 2017;377:523-33 that reported data at a median total treatment duration of 8.2 months:

- The median progression free survival (PFS) was 7.0 months olaparib vs. 4.2-months TPC (HR for disease progression or death, 0.58; 95% CI, 0.43 to 0.80; P<0.001). The Committee considered this was statistically significant.
- At 12 months, 25.9% olaparib vs 15.0% TPC were free of progression or death

8.28.4. The Committee noted the following publications that reported data from the OlympiaD trial:

- Robson et al. Eur J Cancer 2019:120:20-30.
- Senkus et al. Int J Cancer. 2023;153:803-14.

8.29. The Committee considered capecitabine was most common first line chemotherapy option, whilst eribulin is not routinely used in New Zealand.

8.30. The Committee considered the trial enrolled an equal proportion of individuals with TNBC and HR+ cancers. The Committee considered this was not representative of the New Zealand population.

8.31. The Committee further considered that due to the high proportion of individuals with TNBC, that additional follow up time is unlikely to provide further clarity in the OS data due to the high mortality rate of TNBC and subsequent decreasing patient numbers over time.

8.32. The Committee noted approximately 70% of the trial population had had prior chemotherapy, with very few having exposure to pembrolizumab, or CDK4/6 inhibitors including palbociclib, which are both funded in New Zealand.

8.33. The Committee considered overall the trial population were young. The Committee considered individuals with *BRCA*m were typically younger than the overall breast cancer population.

8.34. The Committee considered overall olaparib did not result in any significant increases in toxicity compared to TPC.

8.35. Overall, the Committee noted the OS benefit from olaparib was not significant in the majority of individuals in the trial, however, was statistically significant in individuals in first line treatment who had not been previously treated with chemotherapy. The Committee considered this was a post-hoc, unpowered subgroup analysis, and the number of individuals included was very small.

8.36. The Committee overall considered there was good evidence of PFS benefit.

Somatic *BRCA* and germline *PALB2* mutations

8.37. The Committee noted TBCRC 048, an investigator-initiated proof of principle phase two trial (Tung et al. J.Clin.Oncol.2024; 42.16.suppl1021).

- The Committee considered that there were small numbers of individuals included in the trial (g*PALB2* n=24, s*BRCA* n=30)
- The Committee noted the results reported for the g*PALB2* cohort - 18 confirmed responses for objective response rate (ORR) of 75% (80% CI: 60.2%-86.3%); clinical benefit rate (CBR) at 18 weeks was 83.3% (90% CI: 65.8%-94.1%). Median PFS was 9.6 months (90% CI: 8.3-12.4). Median duration of response (DOR) was 7.1 months (90% CI: 5.6-11.0).
- The Committee noted the results reported for the s*BRCA1/2) cohort* - 11 confirmed responses for ORR of 36.7% (80% CI: 24.8%-50%). CBR was 53.3% (90% CI: 37%-69.2%) and median PFS was 5.6 months (90% CI: 3.0-8.3). Median DOR was 12.4 months (90% CI: 4.3-not reached). One additional person with a s*BRCA*m had a partial response, which was not confirmed.

8.38. The Committee noted LUCY, an open-label, single-arm trial. (Balmana et al. Breast Cancer Res Treat 2023;204:237–48, Gelmon et al. Eur J Cancer. 2021:152:68-77).

8.38.1. The Committee considered there were small number of individuals with somatic *BRCA* mutations (gBRCAm, *n* = 253, sBRCAm, *n* = 3)

8.38.2. The Committee noted the final analysis reported for g*BRCA*m the median investigator-assessed PFS (primary endpoint) was 8.18 months, and median OS was 24.94 months.

8.39. The Committee noted a retrospective cohort analysis of a database of 46,000 people, of which 71 had a germline *BRCA*m, 31 had a somatic *BRCA* or germline *PALB2*m treated with a PARPi (Batalini et al. JCO Precis Oncol. 2023;7:e2300091). The Committee considered the outcomes in individuals with a germline or somatic mutation were numerically similar in terms of real world PFS and OS.

8.40. Overall, the Committee considered there was a lack of high-quality evidence to support the health benefit of olaparib in the treatment of somatic *BRCA* or germline *PALB2* HER2- breast cancers. The Committee noted the number of individuals with the mutations included in the studies were very small and considered there was unlikely to be further high quality, randomised clinical trial evidence for individuals with these mutations treated with olaparib.

Suitability

8.41. The Committee noted olaparib is administered as an oral treatment which can be taken by the person at home. Whilst this is an increase in pill burden compared to other treatments, it would reduce the time taken to travel to infusion services, and receive treatments compared to other chemotherapeutic agents. The Committee considered this would be especially beneficial to those in rural areas or that are located further from infusion services.

8.42. The Committee considered the pilot screening program for *BRCA* testing would need to expand out to standard of care to ensure equitable access for the New Zealand population, with the current system constricted to specific regions.

Cost and savings

8.43. The Committee considered there was some variation in how individuals are categorised as ER positive, with some classifying ER expression as ≥1% whilst others were ≥5 or 10%. Therefore, there may be some variation in the population size.

8.44. The Committee considered it would be reasonable to double the size of the historical data cohort in New Zealand that were identified as *BRCA1/2* positive due to the current process undertesting the population, leading to an approximate 50% under-diagnosis rate.

8.45. The Committee considered there may also be a prevalent population of individuals with ER+ cancer that have not been currently tested but may subsequently be tested if a *BRCA1/2* targeting agent is funded.

8.46. The Committee considered there was a lack of evidence to determine if there was a health benefit to the use of a PARP inhibitor prior or post immune checkpoint inhibitor treatment. The Committee considered whilst uncertain, it was likely pembrolizumab would be used in preference in individuals with TNBC due to the overall survival benefit and clinician familiarity with the treatment. However, considered for HR+ populations, then olaparib may be used in first line.

8.47. The Committee considered there was a paucity of high-quality evidence to assume similar results between individuals with germline and somatically derived *BRCA* mutations. The Committee noted evidence from ovarian cancers that reported there was a step wise decrease in the efficacy of olaparib when comparing germline to somatic *BRCA* mutations, and therefore the Committee considered it would be appropriate to decrease the health benefits by approximately 50% when considering somatic *BRCA* mutated breast cancers.

8.48. The Committee considered that there was no quality-of-life benefit from olaparib treatment that is independent of PFS.

8.49. The Committee considered that expansion of the pilot testing program for *BRCA* would be necessary if olaparib were funded and represent an increased health system cost.

Funding criteria

8.50. The Committee considered there was a lack of evidence on olaparib retreatment in the metastatic setting after use in the early breast cancer. The Committee considered it would be appropriate to restrict olaparib use to once per patient lifetime.

8.51. The Committee considered olaparib treatment should be restricted to two years or until disease progression.

8.52. The Committee considered that it would be appropriate to follow the ESMO guidelines when considering the treatment paradigm if olaparib were funded.

Summary for assessment

8.53. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for olaparib if it were to be funded in New Zealand for *BRCA*m or *PALB2*m HER2-negative locally advanced or metastatic breast cancer. 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	*BRCA*m HER2-negative locally advanced or metastatic breast cancer *PALB2*m HER2-negative locally advanced or metastatic breast cancer * Line of therapy dependent on subpopulation. For HER2-/HR+ mBC and TNBC PD-L1 positive, treatment would be 2L/3L. For TNBC PD-L1 treatment may be in 1L/2L/3L
Intervention	Olaparib 300mg taken twice daily for two years or until disease progression

Comparator(s)	• Chemotherapy • Pembrolizumab Palbociclib or ribociclib
Outcome(s)	PFS. 7.0 months olaparib vs. 4.2 month TPC (HR for disease progression or death, 0.58; 95% CI, 0.43 to 0.80; P<0.001) Robson et al. N Engl J Med 2017;377:523-33 • No prior chemotherapy for mBC (1L) HR 0.56, (95% CI 0.34-0.98) • Prior chemotherapy for mBC (2L/3L HR 0.65, (95% CI 0.47-0.91) OS. Median OS was 19.3 months for olaparib vs 17.1 months for TPC. HR 0.89, (95% CI 0.67-1.18) Robson et al. Eur J Cancer. 2023:184:39-47 • No prior chemotherapy for mBC (1L) Median OS was 22.6 months for olaparib vs 14.6 months for TPC. HR 0.55, (95% CI 0.33-0.95) • Prior chemotherapy for mBC (2L/3L) Median OS was 18.8 months for olaparib vs 17.2 months for TPC. HR 1.05, (95% CI 0.76-1.47)
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. Olaparib for the treatment of early high risk *BRCA*m HER2 negative breast cancer after neoadjuvant or adjuvant chemotherapy

Application

9.1. The Committee reviewed the application for olaparib for the treatment of early high risk *BReast CAncer* mutated (*BRCA*m) HER2 negative (HER2-) breast cancer after neoadjuvant or adjuvant chemotherapy.

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 olaparib for the treatment of early high risk *BRCA*m HER2 negative breast cancer after neoadjuvant or adjuvant chemotherapy application be funded with a **high priority** within the context of treatment of malignancy subject to the following Special Authority criteria:

> **Initial application – (early breast cancer, adjuvant)** only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
>
> 7. Either:
> 7.1. Individual has Stage II or III breast cancer that does not express ER, PR or HER2 IHC3+ or ISH+ (including FISH or other technology); or
> 7.2. Individual has Stage II or III breast cancer that is confirmed as hormone receptor positive and HER2- negative, and
> 8. Individual has a class 4 or 5 BRCA1 or BRCA2 gene mutation; and
> 9. Individual has undergone surgical resection; and
> 10. Either:
> 10.1. Individual has completed systemic (neo)adjuvant chemotherapy; or
> 10.2. Individual has undergone adjuvant endocrine therapy or neoadjuvant chemotherapy followed by endocrine therapy; and
> 11. Adjuvant treatment with olaparib to be commenced within 12 weeks of completing other therapy including surgery, radiotherapy or chemotherapy; and
> 12. Olaparib to be used in combination with endocrine therapy in individuals with hormone receptor positive breast cancer; and
> 13. Olaparib to be discontinued at disease recurrence; and

14. Total adjuvant treatment with olaparib must not exceed 12 months

Renewal application – (early breast cancer, adjuvant) only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:
4. No evidence of disease recurrence; and
5. Olaparib to be discontinued at disease recurrence; and
6. Total adjuvant treatment with olaparib must not exceed 12 months and
7. Olaparib to be used in combination with endocrine therapy individuals with hormone positive breast cancer.

9.4. In making these recommendations, the Committee considered:

- The high health need of individuals with early high risk *BRCA*m HER2- breast cancer
- The increased suitability from an oral formulation compared to intravenous chemotherapeutic regimes
- Individuals with *BRCA*m not benefiting from the available funded treatments
- The increase in overall survival from olaparib treatment.

Discussion

Māori impact

9.5. The Committee discussed the impact of funding olaparib for the treatment of early high risk *BRCA*m HER2- breast cancer after neoadjuvant or adjuvant chemotherapy on Māori health areas of focus | Hauora Arotahi and Māori health outcomes.

9.5.1. The Committee noted the treatment of breast cancer is an area of health focus.

9.5.2. The Committee considered whilst there was evidence that Māori have worse health outcomes from early high risk HER2- breast cancer there is no data to indicate there would be any difference in health outcomes from olaparib treatment.

9.5.3. The Committee also considered there was a lack of data to suggest Māori have higher rates of *BRCA*m, however noted reference databases to identify pathogenic variants were predominantly comprised of European data and therefore may not identify pathogenic variants for Māori.

Populations with high health needs

9.6. The Committee discussed the health need(s) of early high risk HER2- breast cancer 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 olaparib and considered:

9.6.1. The Committee considered that the oral tablet formulation of olaparib would make it easier for groups experiencing health inequities to access treatment compared to intravenous infusions.

9.6.2. The Committee considered there was a lack of data to suggest Pacific peoples or other ethnic groups have higher rates of *BRCA*m however noted reference databases to identify pathogenic variants were predominantly comprised of European data and therefore may not identify pathogenic variants for non-Europeans.

Background

9.7. The Committee noted olaparib is funded for the second line treatment of high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer in individuals with a germline *BRCA1/2*m.

Health need

9.8. The Committee noted the application focussed on individuals with high-risk early breast cancer that have a *BRCA*m, irrespective of hormone receptor (HR) status, excluding individuals with HER2 positive disease. Therefore, discussion focusses on individuals with both HR positive and triple negative (TNBC) breast cancer. The Committee noted the health need of individuals with TNBC has been recently discussed by the Committee in October 2023.

9.9. The Committee noted the health need of individuals with *BRCA*m cancers was discussed at the meeting when considering olaparib in the metastatic setting.

9.10. The Committee considered the prevalence of *BRCA*m high-risk early breast cancer in the New Zealand population was uncertain.

9.11. The Committee considered the aim of adjuvant treatment is to increase disease cure rates by providing additional treatments prior to, and concurrent with, systemic therapies.

9.12. The Committee considered the eligible population, those with early high risk *BRCA*m breast cancer, would only be identified if there was adequate, nationwide, rapid screening available. The Committee considered this was not available at present.

9.13. The Committee considered the new mainstreaming pilot may improve the efficiency of testing however considered it was not implemented nationwide yet. The Committee considered there were additional testing challenges due to restricted laboratory capacity.

9.14. The Committee noted the European Society for Medical Oncology (ESMO) guidelines for early TNBC and HR+ breast cancer. The Committee noted olaparib is used in preference to capecitabine. The Committee noted olaparib was offered to all individuals with *BRCA*m cancer unless they experienced pathological complete response after neoadjuvant chemotherapy or had low risk disease.

Special Interest Group Feedback

9.15. The Committee noted Pharmac staff reached out to the New Zealand Breast Cancer Special Interest Group (BSIG) to receive clinical input on a range of applications. The SIG noted that ‘in patients with BRCA pathogenic variants and triple negative breast cancer adjuvant olaparib is treatment of choice (rather than capecitabine) due to specific trial data with a targeted treatment to a detected biomarker. Adjuvant CDK4/6 inhibitor are not recommended in this group. Guidelines and safety data suggest pembrolizumab should be given alongside olaparib in this group as there was an EFS benefit in those who did not get a pCR (56% vs 67%). There have been no randomised trials looking at the combination of olaparib and pembrolizumab in this population.’

9.16. The Committee noted the SIG considered that the use of olaparib would be supported by the roll out of mainstream genetic testing. The SIG concluded that mainstreaming was more vital in identifying those who would be eligible for adjuvant olaparib as this is a more time sensitive treatment decision and results are needed promptly to identify those suitable for treatment.

9.17. The Committee noted that an application for pembrolizumab in combination with olaparib has not been received.

Health benefit

9.18. The Committee noted the OlympiA, phase three, double-blinded, placebo-controlled study (N=1836) that compared olaparib to placebo. The Committee noted that all individuals had a germline *BRCA1/2*m.

9.18.1. The Committee noted that final overall survival (OS analysis) is estimated to be 15 years from first patient randomised whilst the pre-specified interim analysis (IA) was 10 years after first patient randomised.

9.18.2. The Committee noted results at median follow up of 6.1 years presented at the 2024 San Antonio Breast Cancer Symposium provided by the supplier (Garber et al. Clin Cancer Res 2025;31(12 Suppl):GS1-09). The Committee noted no significance testing was performed at this time point. The Committee noted the following results:

- Primary endpoint: 6-year invasive disease-free survival (IDFS): 79.6% vs 70.3% Olaparib vs placebo difference 9.4% (95% CI 5.1%, 12.7%). Stratified hazard ratio (HR) 0.65 (95% CI: 0.53, 0.78). By HR status: TNBC Stratified HR 0.652 (95% CI: 0.526, 0.805). ER/ and or PgR positive: Stratified HR 0.681 (95% CI: 0.437, 1.051)

- Secondary endpoint: 6-year distant disease-free survival (DDFS): 83.5% vs 75.7% olaparib vs placebo respectively, difference 7.8% (95% CI 3.8%, 11.5%).

- Stratified HR 0.65 (95% CI: 0.53, 0.81) 6-year OS: 87.5 vs 83.2% olaparib vs placebo respectively, difference 4.4% (95% CI: 0.9%, 6.7%). Stratified HR 0.72 (95% CI: 0.56, 0.93).

9.18.3. The Committee noted Geyer et al. Ann Oncol. 2022 ;33:1250-68 that reported results at median follow up of 3.5 years.

9.18.4. The Committee noted Tutt et al. N Engl J Med. 2021;384:2394-405 that reported results at median follow up of 2.5 years.

9.18.5. The Committee noted no individuals received additional immunotherapy due to it being unavailable at the time the trial was performed.

9.18.6. The Committee noted patients were recruited prior use of adjuvant capecitabine for individuals with TNBC which is now standard of care, and the trial approach of adjuvant immunotherapies which is still being defined. Therefore, the Committee considered the comparator arm does not accurately reflect the current practice in New Zealand due to the timing of the trial recruitment.

9.18.7. The Committee noted the majority of individuals in the trial had TNBC, with a much smaller proportion having HR+ breast cancer.

9.18.8. The Committee considered the baseline characteristics of the trial were balanced.

9.18.9. The Committee considered approximately 50% of the trial had received neoadjuvant chemotherapy, with the other 50% receiving adjuvant chemotherapy. The Committee noted approximately 25% had received a platinum-based chemotherapy which is currently standard of care in neoadjuvant chemotherapy for TNBC.

9.18.10. The Committee noted the majority of the individuals had a *BRCA1*m (72.3%), with 27.2% having a *BRCA2*m and 0.4% having a mutation in both genes.

9.18.11. The Committee noted the significant improvements in IDFS and DDFS for olaparib compared to placebo were maintained from results at a median follow up of 2.5 years to a median follow up of 6.1 years. The Committee noted that OS was significant at a median 6.1 years of follow up. The Committee noted no additional safety signals were noted overtime.

9.18.12. The Committee noted there was a reduction in the development of new primary tumours when treated with olaparib compared to placebo (4.9% vs 7.5% respectively) in a group of individuals who are at a high risk of new tumour development.

9.19. The Committee noted Ganz et al. J Clin Oncol. 2024;42:1288–1300 reported quality of life results from the OlympiA trial. The Committee noted the following results:

9.19.1. Individuals who received olaparib experienced higher levels of fatigue at 6 and 12 months however, the difference was not statistically significant and were reduced by 18 to 24 months. The Committee considered increases in nausea and vomiting reported at 6 and 12 months were also resolved by 18 and 24 months of follow up.

9.20. The Committee considered that overall olaparib provides a significant and evolving OS gain for treatment of early high risk breast cancer. The Committee considered the benefits in OS were meaningful, as well as prolonging IDFS and improving quality of life.

9.21. The Committee considered the adverse effects of olaparib were modest, with the most common side effect anaemia, and overall, the treatment was well tolerated.

9.22. The Committee considered the trial was robust, well designed, and applicable to the New Zealand context, however noted capecitabine which was not included in the comparator arm of the study is used as standard of care for individuals with TNBC.

9.23. The Committee noted no trials had assessed olaparib in combination with other adjuvant therapies including pembrolizumab and capecitabine.

9.23.1. The Committee noted there was a significant health benefit of neoadjuvant followed by adjuvant pembrolizumab treatment in the early PDL-1 expressing TNBC. The Committee considered anecdotal evidence that some individuals in New Zealand received neoadjuvant immunotherapy with the aim of achieving pathological complete response. The Committee noted no trials had been performed to investigate olaparib with concurrent immune checkpoint inhibitor treatment, however safety data suggests that this would be possible.

9.23.2. The Committee noted the CREATE-X trial reported an OS benefit for capecitabine in the treatment of TNBC with residual disease. The Committee considered there was no safety or efficacy data on the combination of olaparib with capecitabine in early breast cancer however the OlympiAD trial that evaluated the effects of olaparib in metastatic breast cancer suggested superiority for olaparib compared to chemotherapy monotherapy. The Committee noted capecitabine was the most common chemotherapy used in the metastatic setting.

Suitability

9.24. The Committee considered that the oral tablet formulation of olaparib would make accessing treatment easier compared to chemotherapies that required intravenous infusions.

Cost and savings

9.25. The Committee considered that it was reasonable, based on the available evidence, to assume there was a survival advantage from adjuvant olaparib treatment.

9.26. The Committee considered it was reasonable to assume the same treatment benefit in those who are HR+ compared to TNBC, as well as those who had previously received a platinum-based chemotherapy. The Committee considered these groups were very small within the OlympiA trial however no differences were observed in the subgroups.

9.27. The Committee considered that based on their clinical experience, CDK4/6i are less effective than olaparib in those with *BRCA*m, and that olaparib would likely offer a benefit over these treatments. The Committee noted Condorelli et al. Ann Oncol. 2018 1:640-45 and Arun et al. Br J Cancer. 2024;131:1400-14 and considered the reduced efficacy of CDK4/6i may be due to a mutation in the retinoblastoma 1 gene (RB1) that also occurs in individuals with a *BRCA*m which confers a reduction in the efficacy of CD4/6i in these tumours. Olaparib would also be preferred to CDK4/6i if both were funded. However, the Committee considered that there was no evidence to inform the magnitude of benefit of olaparib over CDK4/6i in this setting and therefore this benefit was as yet not quantified. The Committee noted ESMO guidelines advise against concurrent use of CDK4/6i and olaparib due to overlapping toxicity profiles.

9.28. The Committee noted that ongoing endocrine therapy was not included in the comparator arm of the OlympiA trial for individuals with HR+ disease. The Committee considered approximately 10% of individuals with a *BRCA* mutation would have HR+ disease.

9.29. The Committee noted that the key evidence did not include adjuvant capecitabine in the comparator arm. The Committee considered that it was common for capecitabine to be used in the adjuvant setting for people with TNBC who did not experience a pathological complete response to neoadjuvant treatment. The Committee therefore considered that the benefit of olaparib may be slightly smaller than that observed in the key evidence. However, the Committee also considered that there is some uncertainty in the benefit of adjuvant capecitabine, in this population.

9.30. The Committee considered, based on clinical experience, that plausibly 80% of people with a *BRCA*m may be high-risk, but that this was highly uncertain and may need to be validated further.

9.31. The Committee considered up to 50% of individuals with a *BRCA*m are not detected in New Zealand. The Committee considering the testing capacity is not adequate to test all individuals with early breast cancer currently and considered the uptake of *BRCA* testing would be uncertain based on the laboratory capacity in New Zealand.

9.32. The Committee considered the annual rate of disease relapses over the first 3-5 years after diagnosis is likely to reduce with time for those with TNBC, but not for those with HR+ breast cancer. The Committee noted that most TNBC relapses occur relatively early, whilst HR+ tumours can relapse much later.

Funding criteria

9.33. The Committee considered individuals with somatic mutations were not included in the OlympiA trial and were not tested for in the adjuvant setting. The Committee noted that olaparib for somatic *BRCA*m early breast cancers were not included in the ESMO guidelines and therefore considered it was appropriate to restrict the treatment of olaparib to individuals with germline *BRCA*m.

9.34. The Committee considered that if olaparib and pembrolizumab were both funded for eTNBC, that it may be common for people to receive neoadjuvant treatment with pembrolizumab followed by adjuvant treatment with olaparib. The Committee considered that there was currently no evidence to inform the relative benefit of adjuvant pembrolizumab, either alone or compared to adjuvant olaparib, but

considered that based on clinical experience, it was plausible that much of the effect of pembrolizumab was based on the neoadjuvant component.

9.35. The Committee considered it would be reasonable to restrict the use of olaparib use in the metastatic setting if used in the adjuvant setting. The Committee considered that there was limited evidence to inform the benefit that PARPi retreatment may offer.

Summary for assessment

9.36. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for olaparib if it were to be funded in New Zealand for adjuvant treatment of early high-risk *BRCA*m breast cancer. 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	People with early high risk HER2–negative breast cancer with a *BRCA* mutation who have received standard of care local and systemic treatments.
Intervention	Olaparib 600 mg daily (300 mg twice daily) for up to 12 months, or until disease recurrence, unacceptable toxicity, or death. In the TNBC subgroup, olaparib is intended to be used as monotherapy following completion of neoadjuvant or adjuvant chemotherapy and other standard local treatments (e.g., surgery and radiotherapy). In the HR+ subgroup, olaparib is used in combination with ongoing endocrine therapy, which forms part of the standard of care in this population.
Comparator(s) (NZ context)	TNBC: Adjuvant capecitabine* and/or observation (i.e., no further active treatment following completion of standard local and systemic therapy). HR+/HER2-negative: Ongoing endocrine therapy as part of standard care. *Not allowed in the OlympiA trial, but expected among New Zealand patients who do not experience a complete pathological response to surgery
Outcome(s)	After 6.1 years median follow up: • Improved IDFS - 79.6% vs 70.3% olaparib vs placebo; difference 9.4% (95% CI 5.1%, 12.7%). Hazard ratio: 0.65 (95% CI: 0.54, 0.78). • Improved OS based on available evidence - 87.5 vs 83.2% olaparib vs placebo respectively, difference 4.4% (95% CI: 0.9%, 6.7%). Hazard ratio: 0.73 (95%CI: 0.56, 0.93). Uncertainty in extent to which use of adjuvant capecitabine in New Zealand among those with TNBC would reduce the benefit of olaparib in this subgroup.

Table definitions:

Population: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)

Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).

Comparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.

10. CDK4/6 inhibitors (abemaciclib and ribociclib) for the adjuvant treatment of HR positive, HER2 negative early breast cancer

Application

10.1. The Committee reviewed the application for cyclin dependent kinase 4/6 inhibitors (CDK4/6i) (abemaciclib and ribociclib) for the adjuvant treatment of hormone receptor (HR+) positive, human epidermal receptor 2 negative (HER2-) early breast cancer (eBC).

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

Recommendation

10.3. The Committee **recommended** that abemaciclib for the adjuvant treatment of HR positive, HER2 negative early breast cancer be funded with a **high priority** within the context of treatment of malignancy.

10.4. The Committee **recommended** that ribociclib for the adjuvant treatment of HR positive, HER2 negative early breast cancer be funded with a **medium priority** within the context of treatment of malignancy.

10.5. Both recommendations are subject to the following Special Authority criteria:

> **Ribociclib / Abemaciclib**
> **Initial application (breast cancer, adjuvant)** only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
>
> All of the following
>
> 1. Individual has Stage II or III hormone receptor positive, HER2-negative breast cancer; and
> 2. The cancer is at high risk of recurrence at initiation of CDK4/6i treatment*; and
> 3. Individual has undergone surgical resection; and
> 4. Individual has not been treated with endocrine therapy for more than 6 months prior to commencing CDK4/6i treatment; and
> 5. Abemaciclib/Ribociclib must be used in combination with endocrine therapy; and
> 6. Abemaciclib/Ribociclib to be discontinued at disease recurrence and total adjuvant treatment must not exceed two/three years
>
> * high risk defined as being any of: (a) cancer cells in at least 4 positive axillary lymph nodes, (b) cancer cells in 1 to 3 positive axillary lymph nodes plus at least one of: (i) tumour size of at least 5 cm in size, (ii) grade 3 tumour histology (on the Nottingham grading system)
>
> **Ribociclib / Abemaciclib**
> **Renewal (breast cancer, adjuvant)** only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
>
> All of the following
> 1. There is no evidence of disease recurrence; and
> 2. Abemaciclib/Ribociclib must be used in combination with endocrine therapy; and
> 3. Abemaciclib/Ribociclib to be discontinued at disease recurrence and total adjuvant treatment must not exceed two/three years

10.6. In making these recommendations, the Committee considered:

- The high health need of individuals with high-risk early breast cancer
- Abemaciclib offers a greater survival benefit, with longer term follow up than ribociclib
- The differing side effect profiles between abemaciclib and ribociclib
- Both treatments are an oral formulation which offers suitability benefits.

Discussion

Māori impact

10.7. The Committee discussed the impact of funding abemaciclib and ribociclib for the adjuvant treatment of HR+, HER2- eBC on Māori health areas of focus | Hauora Arotahi and Māori health outcomes.

10.7.1. The Committee noted the reported percentage of breast cancers that are HR+/HER2- is similar in Māori at 74.7% compared to New Zealand European 75.2% (Breast cancer foundation NZ 30,000 voices, 2022).

10.7.2. The Committee noted the treatment of breast cancer is a Hauora Arotahi (Pharmac Māori Health Areas of Focus).

10.7.3. The Committee noted there is a higher incidence of breast cancer in Māori, that is diagnosed at a later stage. The Committee note that Māori have worse health outcomes compared to New Zealand Europeans.

10.7.4. In addition, the Committee noted that Māori women are approximately 5 years younger at diagnosis than non-Māori women.

Populations with high health needs

10.8. The Committee discussed the health need(s) of HR+, HER2- eBC 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 abemaciclib and ribociclib and noted:

10.8.1. There is a higher incidence of breast cancer for Pacific people, that is diagnosed at a later stage. The Committee note that Pacific people have worse health outcomes compared to New Zealand Europeans.

10.8.2. That those from higher deprivation quintiles have worse breast cancer outcomes.

Background

10.9. The Committee noted that ribociclib, a cyclin dependent kinase inhibitor (CDK4/6i) is funded for HR+/HER2- advanced or metastatic breast cancer.

Health need

10.10. The Committee noted that the health need of individuals with HER2-, triple negative breast cancer (TNBC) eBC was recently discussed in October 2023.

10.11. The Committee noted HR+ HER- is the most common subtype of breast cancer, which accounts for approximately 70% of all breast cancer cases (American Cancer Society. Breast Cancer Facts & Figures 2019-2020, Howlader et al. J Natl Cancer Inst. 2014;106:dju055, Breast cancer foundation NZ 30,000 voices, 2022).

10.12. The Committee noted this type of cancer is known to have a good response to hormone therapy and favourable prognosis (Iwamoto et al. Chin Clin Oncol. 2020;9:27), with the Breast Cancer Foundation New Zealand (BCFNZ) reporting a 92% 10 year survival rate for individuals.

10.13. The Committee noted approximately 30% of individuals with eBC present with disease recurrence during follow-up. More than 50% of recurrences occur within the first five years, peaking at two years (Cheng et al. Cancer Epidemiol Biomarkers Prev. 2012;21:800-9). The risk is higher in individuals with node positive disease (Colleoni et al. J Clin Oncol. 2016;34:927-35). Of all recurrences, around 10% to 20% are isolated locoregional recurrences, while the majority (60% to 70%) are distant

metastases (Christiansen et al. Acta Oncol. 2008;47:691-703). Median overall survival (OS) of individuals with HR+, HER2- advanced breast cancer is 38.4 months (Meegdes et al. Lancet Reg Health Eur. 2023:26:100573).

10.14. The Committee considered individuals with HR+ HER2- eBC at a high risk of recurrence have similar outcomes to individuals with TNBC and therefore the impacts on heath related quality of life and effects on the whānau of individuals should be considered to be similar.

10.15. The Committee noted that the five-year rates of invasive disease-free survival (IDFS), distant relapse free survival (DRFS) and overall survival (OS) are lower for individuals with high-risk disease compared to low medium risk disease. (73.9%, 75.9%, 91.0% vs 86.1%, 87.7%, 94.9% respectively) (Loponen et al. J Health Econ Outcomes Res. 2025;12:252-60).

10.16. The Committee noted a supplier provided patient survey identified that 96% of individuals acknowledged living with breast cancer had some sort of negative effect on their mental health, with 63% reporting a very significant negative effect (Project Shirley, Novartis, ribociclib submission). Of individuals with high risk eBC 85% reported their mental health was significantly negatively impacted by living with breast cancer, with 95% expressing their fear of recurrence was their greatest concern.

10.17. The Committee noted that individuals with early-stage HR+, HER2- breast cancer are treated with curative intent; treatment typically includes surgery followed by radiotherapy. The Committee noted some individuals may receive neoadjuvant chemotherapy however most are treated with adjuvant systemic therapy after surgery. The therapy received is based on individual risk of disease relapse recurrence, and predicted sensitivity to available systemic therapies (Cancer Australia, 2020 Guidance for the management of early breast cancer).

10.18. The Committee noted individuals are often prescribed endocrine therapy (ET) for 5-10 years following primary treatment (Breast Cancer Aotearoa Coalition, New Zealand statistics 2020), however whilst almost all who were eligible commenced ET, studies have shown that approximately only half of individuals have high adherence over the treatment duration (Breast cancer foundation NZ 30,000 voices, 2022).

10.19. The Committee noted the European Society for Medical Oncology (ESMO) guidelines for the treatment of HR+ HER2- eBC.

10.20. The Committee noted the percentage of breast cancers that are HR+/HER2- is similar in Māori at 74.7% compared to NZ European 75.2% (Breast cancer foundation NZ 30,000 voices, 2022).

Special Interest Group and Consumer Feedback

10.21. The Committee noted that Pharmac staff had reached out to the New Zealand Breast Cancer Special Interest Group (BSIG) to seek their clinical input on a range of breast cancer related applications including abemaciclib and ribociclib for this population group.

10.22. The BSIG considered both applications should be highly prioritised for consideration by the committee and noted there was SIG consensus for one funded CDK4/6i in high-risk HR+ disease. The SIG also noted that it would support the use of the criteria for high risk as per the MonarchE trial, as this group of patients would receive the most benefit.

10.23. The Committee noted it had received a consumer application, and a consumer provided letter that provided support to this funding proposal and patient lived experience of the disease. The Committee noted the application included a petition

with over 2000 signatures. The Committee wished to express their sincere gratitude to the individuals and recognised that sharing such stories is not easy.

Health benefit

Abemaciclib

10.24. The Committee noted MonarchE, an open label, randomised, phase III trial, that compared abemaciclib plus ET with ET monotherapy (N=5637).

10.25. The Committee noted Johnston et al. Ann Oncol 2025:S0923-753;04948-8 that reported the trial results with a median follow up of 76.2 months:

- For abemaciclib the hazard ratio (HR) for death was 0.842, 95% confidence interval (CI) 0.722-0.981, *P* = 0.027], meeting the prespecified boundary for significance.
- The seven-year OS was 86.8% with abemaciclib and 85.0% with ET (absolute difference, 1.8%).
- The seven-year IDFS was 77.4% with abemaciclib and 70.9% with ET (absolute difference, 6.5%) and 7-year DRFS were 80.0% and 74.9% (absolute difference, 5.1%).
- The number of deaths due to breast cancer was reduced with abemaciclib (10.5% ET vs 7.9% abemaciclib) as well as the number living with metastatic disease (9.4% ET vs 6.4% abemaciclib).

10.26. The Committee noted Rastogi et al. J Clin Oncol. 2024;42:987-93. that reported the five year results:

- Abemaciclib had a hazard ratio (HR) of 0.680 (95% CI, 0.599 to 0.772) IDFS and 0.675 (95% CI, 0.588 to 0.774) for DRFS.
- Five-year absolute improvement in IDFS and DRFS rates of 7.6% and 6.7%, respectively, compared with rates of 6% and 5.3% at 4 years and 4.8% and 4.1% at 3 years.
- Statistical significance was not reached for OS.

10.27. The Committee noted Tolaney et al. Eur J Cancer. 2024:199:113555 that reported patient reported outcomes. The Committee noted that within the abemaciclib arm, meaningful differences for diarrhoea were observed at 3 and 6 months (mean increases of 1.19 and 1.03 points on 5-point scale, respectively). During post-treatment follow-up, patient reported outcomes (PRO) in both arms were similar to baseline.

Ribociclib

10.28. The Committee noted NATALEE, multicentre, randomised, open-label, Phase III trial that compared ribociclib with ET with ET monotherapy (N=5101).

10.28.1. The Committee noted 5-year data provided by the supplier that was presented at ESMO 2025 that reported results with median follow up 62.5 months:

- The IDFS was a 28.4% risk reduction in ribociclib vs nonsteroidal aromatase inhibitor (NSAI) (hazard ratio (HR) = 0.716 (0.618, 0.829, p-value <0.0001)) compared to final IDFS analysis (HR 0.749 (0.628-0.892)) and consistent with 4-yr analysis (HR 0.715 (0.609-0.840)
- OS remains immature with a HR 0.800 (0.637, 1.003, one-sided p-value 0.026) is observed compared to final IDFS analysis (OS HR = 0.892 (0.661-1.203))

10.28.2. The Committee noted Fasching et al. JAMA Oncol. JAMA Oncol. 2025:e253700 that reported the descriptive exploratory 4 year analysis.

- Median follow-up for IDFS was 44.2 months (range, 0-63 months) that reported a ribociclib benefit over NSAI alone (HR, 0.72; 95% CI, 0.61-0.84), with 3-year IDFS rates of 90.8% vs 88.1% (difference, 2.7 percentage points) and 4-year rates of 88.5% vs 83.6% (difference, 4.9 percentage points).
- OS data remains immature.

10.28.3. The Committee noted Hortobagyi et al. Ann Oncol 2025;36149-57. that reported the final IDFS analysis.

10.28.4. The Committee noted Slamon et al. N Engl J Med. 2024;390:1080-91.that reported the interim analysis medium duration of follow up of 34 months.

10.28.5. The Committee noted that the definition of high-risk disease differed from the MonarchE trial and included individuals with stage IIA disease with at least one lymph node, and individuals with no nodal involvement but a grade two tumour that were not included in the MonarchE trial. The Committee considered these individuals had a lower stage disease than the MonarchE trial.

10.28.6. The Committee considered there was no difference in IDFS benefit between the subgroups, including in those with stage III disease.

10.28.7. The Committee noted the 5 year OS statistical analysis of the NATALEE trial utilised one sided log rank testing however did not consider this to be appropriate. The Committee considered there were a small number of individuals at the later data points and therefore few conclusions could be drawn from this data at this timepoint.

10.28.8. The Committee noted there were fewer events compared to the MonarchE trial however considered this was expected given the lower threshold for high-risk disease. The Committee also noted there was lower mortality.

10.28.9. The Committee considered overall, whilst there is a benefit in terms of IDFS and DRFS, there is not yet a demonstrable survival advantage compared to ET monotherapy at five years of follow up. The Committee considered this is likely due to the stage and risk baseline characteristics of the patients in the trial. The Committee considered that to provide greater certainty on the benefit of ribociclib in a higher-risk subgroup, Pharmac should request additional information from the supplier of ribociclib on whether there is subgroup data from the NATALEE trial among patients who are higher risk and meet the MonarchE trial criteria.

Any CDK4/6i

10.29. The Committee noted Graff et al. Cancer. 2025;131:e35817 that reported a positive correlation between IDFS and OS in HR+ HER2- eBC. The Committee considered there is a strong correlation between IDFS, a surrogate marker, and OS which was confirmed by the MonarchE trial that reported an improvement in OS after reporting an improvement in IDFS. The Committee considered that the gains in OS were likely to be much lower in percentage terms than the gains observed in IDFS.

10.30. The Committee noted that the trials did not use the same patient selection criteria, or duration of treatment and therefore are not directly comparable. The Committee considered both the MonarchE and NATALEE trials were high quality and applicable to the New Zealand context, but that the patient selection criteria in the MonarchE

trial targeted higher-risk disease, and therefore outcomes in this trial better reflected the outcomes in the intended patient population.

10.31. The Committee considered there were trials underway to assess the health benefit of CDK4/6i treatment in the advanced setting following use in the adjuvant setting. However, given the currently available evidence, the Committee considered there was currently insufficient data to determine if CDK4/6i retreatment is effective, and therefore that it was appropriate to restrict access to once per patient lifetime.

10.32. The Committee considered that while there is no survival advantage yet observed for ribociclib in this setting, it was likely that the differences in outcomes and treatment effect in the trials for ribociclib and abemaciclib were due to differences in the trial patient selection criteria. The Committee considered it was reasonable to assume there was a class effect between CDK4/6i in the adjuvant setting, though the Committee acknowledged the data is stronger for abemaciclib and therefore that there is greater certainty in the survival advantage offered by abemaciclib. The Committee considered that palbociclib appeared to be significantly less effective than both ribociclib and abemaciclib.

10.33. The Committee considered the side effect profiles of CDK4/6i do not represent a large additional burden to individuals and are mostly well tolerated. The Committee considered there is a difference in the adverse effect pattern between abemaciclib and ribociclib. Abemaciclib is known to cause diarrhoea, cytopenia, fatigue, nausea and abdominal pain, whilst ribociclib is additionally associated with prolonged QT intervals, liver function test abnormalities and interstitial lung disease. The Committee considered it would be reasonable to allow individuals to switch between CDK4/6i due to adverse effects, as each have distinct profiles.

10.34. The Committee were made aware of evidence that individuals who underwent abemaciclib dose reductions due to adverse effects including diarrhoea, had similar health benefits and outcomes compared to those who did not undergo a dose reduction.

10.35. The Committee considered that whilst the treatments were administered for two and three years respectively, the treatment effect was likely to persist beyond the duration of duration of treatment. The Committee considered that the available evidence indicated that there was treatment benefit at five and seven years respectively for ribociclib and abemaciclib, though there was little evidence to inform assumptions about treatment waning.

Suitability

10.36. The Committee considered that ribociclib must be kept in the fridge which can be challenging in clinical practice.

10.37. The Committee considered individuals receiving ribociclib would potentially require additional ECGs and liver function tests, which may require additional travel or clinic visits.

Cost and savings

10.38. The Committee considered that the uptake of CDK4/6i in this setting would be rapid. The Committee considered that the uptake of trastuzumab emtansine in early HER2+ breast cancer would be a good proxy for the uptake of CDK4/6i, and that uptake for these treatments would be at least as high as for trastuzumab emtansine, or possibly higher given the more favourable suitability of CDK4/6i.

10.39. The Committee considered that based on experience and published data in advanced disease that abemaciclib would be more widely used if both ribociclib and abemaciclib were funded in this setting.

10.40. The Committee considered if olaparib were funded for individuals with *BRCA1/2* mutations, approximately 20% of individuals with HR+ HER2- eBC, the number receiving adjuvant CDK4/6i would decrease.

10.41. The Committee considered that individuals who are disease free have a near normal health related QOL (HRQOL), whilst this is reduced with either local recurrence or distant metastasis (Criscitello et al Clin Ther. 2021;43:1228-44.e4, Gao et al Qual Life Res. 2023;32:2639-52).

Funding criteria

10.42. The Committee noted that the SIG would support the use of the criteria for high risk as per the MonarchE trial this was defined as ≥4 positive lymph nodes, or 1-3 positive lymph nodes plus either a tumour of ≥5cm or a tumour histology showing grade 3 features.

10.43. The Committee considered that both abemaciclib and ribociclib should be subject to the same Special Authority criteria.

Summary for assessment

10.44. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for abemaciclib and ribociclib if they were to be funded in New Zealand for HR positive, HER2 negative eBC at high risk of recurrence. 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	Individuals with HR positive, HER2 negative eBC at high risk of recurrence. Patient characteristics and selection criteria similar to those in the MonarchE trial.
Intervention	Abemaciclib: 150mg orally twice daily for two years or until disease progression, death or unacceptable toxicity. Abemaciclib is used in combination with ET. Ribociclib: 400mg taken orally once daily for 21 days, followed by 7 days off treatment, for three years or until disease progression, death or unacceptable toxicity. Ribociclib is used in combination with ET.
Comparator(s)	Adjuvant ET alone.

Outcome(s)	**Overall survival:** • **Significant survival advantage with abemaciclib + ET vs ET alone** in MonarchE trial (HR 0.842, 95% CI 0.72-0.98), seven-year OS 86.8% vs 85.0% (Johnston et al. Ann Oncol 2025:S0923-753;04948-8) • **No survival advantage yet observed for ribociclib due to immature data** • **Likely similar OS benefit for abemaciclib and ribociclib** (class effect), with greater uncertainty for ribociclib due to lack of data • OS advantage likely to be lower than IDFS advantage **IDFS:** • **Significant IDFS advantage with abemaciclib + ET vs ET alone (**HR 0.73, 95% CI 0.66-0.82680 (95% CI, 0.599 to 0.772), based on seven-year MonarchE data • **Significant IDFS advantage with ribococlib + ET vs ET alone** in NATALEE (HR 0.749, 95% CI 0.63-0.89) (Hortobagyi et al. Ann Oncol 2025;36149-57) • Likely similar IDFS advantages with abemaciclib and ribociclib
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.	

11. Belantamab mafodotin (Blenrep) for the treatment of relapsed or refractory multiple myeloma (2nd line or later)

Application

11.1. The Committee reviewed the application from GlaxoSmithKline NZ Limited for the use of belantamab mafodotin (Blenrep) for the treatment of relapsed or refractory multiple myeloma (RRMM) for people who have received at least one prior therapy (ie in the second-line setting or later).

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

Recommendation

11.3. The Committee **recommended** that belantamab mafodotin be listed for the treatment of relapsed or refractory multiple myeloma (RRMM) second line or later with a **high priority**, within the context of treatments for malignancy, subject to the following Special Authority criteria:

> Initial application – (Relapsed/refractory multiple myeloma) from any relevant practitioner.
> Approvals valid for 12 months for applications meeting the following criteria:
> All of the following:
> 1. Person has relapsed or refractory multiple myeloma with progressive disease; and
> 2. Person has received at least one prior line of therapy for multiple myeloma; and
> 3. Person has not received prior funded belantamab mafodotin.
>
> Renewal application: Relapsed/refractory multiple myeloma from any relevant practitioner.
> Approvals valid for 12 months where there is no evidence of disease progression.

11.4. In making this recommendation, the Committee considered the following:

11.4.1. The high health need of people with RRMM who have few available treatment options

11.4.2. That in the second line or later, belantamab mafodotin provides a progression-free survival (PFS) benefit and it is reasonable to assume an overall survival (OS) benefit compared with pomalidomide, bortezomib, and dexamethasone (PVd), or compared with pomalidomide and dexamethasone (Pd) in those who cannot have bortezomib, with quality of life (QOL) maintained.

11.4.3. That toxicities associated with belantamab mafodotin (including ocular ones) would be manageable and their monitoring requirements in New Zealand clinical care would likely be less than was required in the clinical trials.

11.5. The Committee considered that it would be relevant to review evidence for the use of daratumumab as a first line treatment for multiple myeloma and noted that Pharmac would welcome a funding application for this.

Discussion

Māori impact

11.6. The Committee considered that the impact of RRMM on Māori health areas of focus | Hauora Arotahi and Māori health outcomes has been described in previous clinical advice records for various treatments for multiple myeloma (refer to the Application Tracker [link]).

Populations with high health needs

11.7. The Committee considered that the health need(s) of people with RRMM 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, have been described in previous clinical advice records for various treatments for multiple myeloma (refer to the Application Tracker [link]).

Background

11.8. The Committee noted that Pharmac and the Advisory Committees have previously considered various treatments for multiple myeloma on many occasions. Refer to the Application Tracker (link) for a list of all applications and proposals considered. The Committee noted that:

11.8.1. Bortezomib is funded for use at any time in the treatment of symptomatic multiple myeloma, without a maximum number of funded treatment cycles.

11.8.2. Applications for carfilzomib for the second- and third-line treatment of RRMM are currently under assessment.

11.8.3. In the past five years, daratumumab has also been considered for RRMM in the second- and third-line settings, with both intravenous (IV) and subcutaneous (SC) formulations considered.

11.9. The Committee noted that in July 2024, as a result of a competitive process for the Principal Supply of lenalidomide and pomalidomide, Pharmac announced funding from 1 August 2024 as follows (link to notification):

11.9.1. Lenalidomide for the first-line treatment of people with either plasma cell dyscrasia (e.g. multiple myeloma) or myelodysplastic syndrome associated with a 5q deletion who have transfusion-dependent anaemia.

11.9.2. Pomalidomide (Pomolide) for people with relapsed/refractory plasma cell dyscrasia as second or later line treatment.

Health need

11.10. The Committee noted the October 2025 letter of support for belantamab mafodotin from Myeloma New Zealand, which provides patient perspectives on the impact of

RRMM, unmet need, current treatments, other considerations, and the impact of belantamab mafodotin. Members agreed that there are few treatment options for people with RRMM in New Zealand compared with other countries and acknowledged concerns about the time taken to fund new medicines for RRMM and the difference in five-year overall survival (OS) in Australia (51%) compared with New Zealand (45%).

11.11. The Committee noted the current treatment paradigm. The Committee considered that first line treatment choices depend on an individual's suitability for an autologous stem cell transplant (autoSCT), and that if lenalidomide is used this might be continued as maintenance or stopped after induction. The Committee noted second line treatment might be pomalidomide (P) with or without bortezomib (V) depending on whether an individual had neuropathy (which would be the main reason not to use bortezomib second line) and considered that approximately two-thirds of people with RRMM would receive pomalidomide with bortezomib and dexamethasone (PVd) second line. The Committee noted that evidence for progression free survival (PFS) with each of these regimens from the corresponding clinical trials was considered by the Committee in 2024.

Health benefit

11.12. The Committee noted that an application for belantamab mafodotin (Blenrep) has been lodged with Medsafe for people with multiple myeloma who have received at least one prior therapy and have relapsed or had disease that was refractory to treatment.

11.13. The Committee noted that belantamab mafodotin is administered as a 30-minute intravenous infusion. When given with Vd (bortezomib and dexamethasone), the starting dose is 2.5 mg/kg every three weeks, or with Pd (pomalidomide and dexamethasone) the starting dose is 2.5 mg/kg for the first cycle then 1.9 mg/kg every four weeks for cycle two and later. After 9 months the average infusion frequency is expected to be every eight to 12 weeks (Mateos et al. Blood Adv. 2025 [online ahead of print]).

11.14. The Committee noted evidence from DREAMM-7: a phase III, open-label, randomised (1:1) trial in 494 patients with MM who had received at least one line of therapy and had disease progression during or after the most recent therapy. Participants received either belantamab mafodotin IV 2.5 mg/kg every three weeks with bortezomib and dexamethasone (BVd), or daratumumab IV 16 mg/kg, bortezomib, and dexamethasone (DVd) (Hungria et al. N Engl J Med. 2024;391:393-407).

11.14.1. The Committee noted that in DREAMM-7, about half had received one prior line and 36-39% had received two or three prior lines, with about 85% having received bortezomib prior and only 1-2% having had daratumumab prior. The Committee considered this means about half were similar to the New Zealand patient population who would be likely to receive belantamab mafodotin (those who had received one prior line), if funded.

11.14.2. The Committee noted that 257 (52%) had prior lenalidomide, 166 (34%) were refractory to lenalidomide, ≤10% had prior pomalidomide, and two-thirds had prior autoSCT. The Committee considered that there would be a slightly higher proportion of patients in New Zealand with prior lenalidomide treatment. However, the Committee considered this prior exposure to other treatments was not substantially different to the New Zealand population who would be likely to receive belantamab mafodotin, if funded, and therefore DREAMM-7 would provide relevant efficacy outcomes for BVd efficacy in the second line.

11.14.3. The Committee noted that after median follow-up of 28.2 months, the primary endpoint of median progression-free survival (mPFS) in DREAMM-7 was 36.6 months (95% confidence interval [CI], 28.4 to not reached) in the BVd group and 13.4 months (95% CI, 11.1 to 17.5) in the DVd group (hazard ratio (HR) for disease progression or death, 0.41; 95% CI, 0.31 to 0.53; P<0.001). The Committee considered this difference reflected a meaningful improvement.

11.14.3.1. The Committee noted that mPFS with DVd was 16.7 months in the CASTOR trial (Spencer et al. Haematologica. 2018;103:2079-87). However, the CASTOR population received less prior treatment and had a lower proportion of lenalidomide-refractory participants compared with DREAMM-7. Members considered this difference in risk might account for the difference in mPFS with DVd between the two trials and that mPFS with DVd in DREAMM-7 should otherwise be considered similar to that in CASTOR.

11.14.4. The Committee noted that overall survival (OS) at 18 months in DREAMM-7 was 84% in the BVd group and 73% in the DVd group; the Committee considered this to be a trend although it was not statistically significant and noted that the median number of events had not yet been reached. At the time of the data cutoff, 54 patients (22%) in the BVd group and 87 patients (35%) in the DVd group had died.

11.14.5. The Committee noted that the proportion of DREAMM-7 participants with adverse events (AEs) grade 3 or higher was 95% with BVd compared with 78% DVd, and that ocular events were more common with BVd than DVd (79% vs. 29%). The Committee noted that ocular events were managed with dose modifications and events of worsening visual acuity mostly resolved.

11.14.6. The Committee noted updated results from DREAMM-7 (Hungria et al. Lancet Oncol.2025;26:1067-80) reported after median follow-up of 39.4 months. Median OS was not reached (NR; 95% CI NR-NR) with BVd and NR (41.0 months-NR) with DVd (HR 0.58; 95% CI 0.43, 0.79; P=0.0002). Members considered that despite the lack of mature OS data, this result showed a promising trend in OS with belantamab mafodotin, which could likely be extrapolated to suggest longer term survival benefits relative to current treatment. The Committee considered that the relative OS benefit in New Zealand would likely be greater than in the trial, noting the known benefit of daratumumab (not currently funded) relative to current New Zealand standard of care (comparator) treatment with PVd.

11.14.7. The most common grade 3 or 4 AE was thrombocytopenia (135/242 [56%] BVd vs 87/246 [35%] DVd) and serious AEs (SAEs) occurred in 129/242 (53%) BVd and 94/246 (38%) DVd, the most common of which was pneumonia.

11.15. The Committee noted evidence from DREAMM-8; a phase III, randomised, open-label trial in 302 people with prior lenalidomide-exposure who had relapsed or refractory myeloma after at least one line of therapy (Dimopoulos et al. N Engl J Med. 2024;391:408-21). The Committee noted that participants received belantamab mafodotin, pomalidomide, and dexamethasone (BPd) vs pomalidomide, bortezomib, and dexamethasone (PVd). The Committee considered this control arm reflected the current second-line treatment for the majority of patients in New Zealand and therefore was highly relevant for comparison of outcomes in our population.

11.15.1. The Committee noted that about half of DREAMM-8 participants had received one prior line of therapy; about one third had received two or three prior lines; ~87% had prior bortezomib; ~25% had prior daratumumab, and previous

autoSCT had occurred in 56-64%. The Committee considered this a heavily pre-treated population with about one third having triple-refractory disease, and that this was similar to the New Zealand population with the exception of anti-CD38 exposure. Members further considered that while DREAMM-8 was the best evidence for health outcomes with BPd in the relevant New Zealand population, the New Zealand population would, if anything, be expected to receive a better response to belantamab mafodotin treatment in this setting due to not having been exposed to daratumumab in earlier treatment lines.

11.15.2. The Committee noted that after median follow-up of 21.8 months, the primary endpoint of 12-month PFS in DREAMM-8 was 71% (95% CI, 63 to 78) with BPd vs 51% (95% CI, 42 to 60) with PVd, HR for disease progression or death, 0.52 (95% CI, 0.37 to 0.73; P<0.001). The Committee noted that median PFS was not reached with belantamab mafodotin vs 13 months with PVd, with the latter being similar to PFS of 11 months as reported in OPTIMISMM. The Committee considered this reflected a substantial improvement compared with currently funded second-line treatment.

11.15.3. The Committee noted that DREAMM-8 OS data were immature, and that 12-month OS was 83% (95% CI, 76 to 88) with BPd and 76% (95% CI, 68 to 82) with PVd (HR, 0.77; 95% CI, 0.53 to 1.14).

11.15.4. The Committee noted that patient-reported outcomes from the global health status and quality-of-life (QOL) domains of the EORTC QLQ-C30 showed no clinically meaningful change from baseline in either treatment group over time in DREAMM-8. The Committee considered that belantamab mafodotin did not lead to any decline in overall health-related QOL.

11.15.5. The Committee noted that the proportion of DREAMM-8 participants with grade 3 or greater AEs was 94% with BPd and 76% with PVd, and that SAEs occurred in 63% and 45%, respectively. The Committee noted that ocular events occurred in 89% with BPd (grade 3 or 4 in 43%) and 30% with PVd (grade 3 or 4 in 2%). Ocular events in the BPd group were managed with belantamab mafodotin dose modification. Ocular events led to treatment discontinuation in 9% with BPd and none with PVd.

11.15.6. The Committee noted updated results from DREAMM-8 presented at the European Haematology Association 2025 Congress (June 12-15 2025, Milan, Italy [poster)). After median 28.01 months the median PFS was 32.6 months (95% CI, 21.1 months-NR) with BPd vs 12.5 months (95% CI, 9.1-17.6 months) with PVd (HR, 0.49; 95% CI, 0.35-0.68). Safety was reported to be consistent with the primary analysis.

11.16. The Committee noted evidence for the efficacy and safety of single-agent belantamab mafodotin versus pomalidomide plus low-dose dexamethasone in patients with relapsed or refractory multiple myeloma from the DREAMM-3 phase III, open-label, randomised study (Dimopoulos et al. Lancet Haematol. 2023;10:e801-12). The Committee considered this was a heavily pretreated group with a median of four prior lines of therapy and that the study included a reasonable number of older patients. The Committee noted that about two-thirds of participants had disease that was refractory to proteosome inhibitor (ie bortezomib) and more than two thirds refractory to an immunomodulatory drug (IMiD; eg lenalidomide or pomalidomide). The Committee noted that median PFS was numerically the same and not statistically significant, and the authors concluded that it was not beneficial to use belantamab mafodotin as a single agent compared with pomalidomide and dexamethasone in this population.

11.17. The Committee considered that the additional outcomes reported from the above DREAMM-3, -7 and -8 trials were trending towards a benefit for all with belantamab mafodotin compared with the respective control groups, with responses being deeper, response rates higher, complete response (CR) and minimal residual disease (MRD) rates quite a bit higher, and duration of response (DOR) being a lot longer with belantamab (DOR 35 months BVd vs 18 months DVd in DREAMM-7; 79% BPd vs 61% PVd at 12 months in DREAMM-8).

11.18. The Committee also noted the following evidence:

- Mateos et al. Blood Adv. 2025: bloodadvances.2025016949
- The impact of patient-reported adverse events on quality of life: An analysis of the DREAMM-7 and DREAMM-8 randomised controlled trials (66th ASH Annual Meeting and Exposition. December 7-10 2024. San Diego, CA, USA)
- Hungria et al. Lancet Haematol. 2025;12:e599-e610
- Hanafin et al. Target Oncol. 2025;20:833-45

11.19. The Committee noted that the most clinically significant risks associated with belantamab mafodotin compared with PVd or Pd were ocular events, and grade 3 thrombocytopenia and neutropenia. The Committee considered that ocular toxicity requiring access to ocular assessments and reduced visual acuity occurred in about one third of participants, although almost all receiving belantamab mafodotin reported some eye symptoms. The Committee considered that dose reduction and/or delay would be expected based on ocular toxicity, and an ophthalmology assessment would not be likely to lead to any different management or compromise efficacy.

11.20. The Committee noted that the evidence for belantamab mafodotin was of good quality being from large, randomised phase III trials. The Committee noted that treatment crossover was not permitted in the clinical trials and considered this appropriate, given that at the time the trials were designed, the evidence didn't support a benefit of belantamab mafodotin in the relapsed setting.

11.21. The Committee noted that QOL of participants was reported to be maintained whilst on treatment with belantamab mafodotin but considered it unclear whether the evidence focus was more on the severe impacts on QOL rather than low-grade QOL differences. The Committee considered that even with ocular toxicities, dose modification and delay would be expected to resolve these issues and it was reasonable to assume QOL would be similar between the belantamab mafodotin and comparator arms.

11.22. The Committee considered that if belantamab mafodotin were funded, there may still be a health need for daratumumab.

11.22.1. The Committee was made aware that daratumumab produces a long significant PFS benefit in the first line setting (reported in the PERSEUS, CASSIOPEIA, and MAIA trials), but an OS benefit in the first line has not yet been reported in transplant-eligible patients. The Committee considered that there would still be a health need for first-line daratumumab even if belantamab mafodotin were funded because daratumumab would provide a longer time to next treatment (via PFS). The Committee considered that this may offer greater benefit for Māori if funded first line given the lower rate of second line myeloma treatment and care for Māori compared with other groups.

11.22.2. The Committee considered that it would be desirable for both daratumumab and belantamab mafodotin to be funded for second line or later treatment of RRMM, as clinician choice depending on toxicity (including ocular toxicity and availability of ocular assessments), patient preferences (eg elderly might

prefer daratumumab), and likely PFS benefit would be the main factors informing choice of treatment.

Suitability

11.23. The Committee considered that the main factors affecting the suitability of belantamab mafotodin for RRMM are the ocular toxicity and management of this requiring modification to the dosing regimen, however, that these were well understood based on clinical trial evidence and real-world experience.

Cost and savings

11.24. The Committee considered that belantamab mafodotin treatment would be initiated at the recommended starting dose but would expect dose decreases to manage ocular toxicity soon after, consistent with DREAMM-8 trial data. However, members considered it possible that the dosing interval could extend (eg out to three-monthly or longer) and ongoing doses could be lower (eg 1mg/kg) based on anecdotal real-world experience. The Committee considered that about 50% of the dose intensity mandated in DREAMM-8 would be the highest dose intensity anticipated. The Committee considered that treatment would continue until disease progression.

11.25. The Committee considered that disease monitoring requirements and their frequencies proposed by the supplier were reasonable although monthly ocular assessment is not funded in New Zealand and could be a barrier to access. However, the Committee considered that ocular assessment may not be needed as frequently as used in the clinical trials. Members noted anecdotal experience from Australia is that an ocular assessment one month after the first dose, then as required when symptoms emerge is reasonable, and that belantamab mafodotin would be administered again once symptoms resolve (median of three months to the next dose at that centre).

11.26. The Committee considered that current usage of belantamab mafodotin through compassionate access programmes indicates both BPd and BVd are used in combination depending on individual patient circumstances, although it is currently used primarily as BVd. The Committee considered that in practice in New Zealand, belantamab mafodotin would be mostly used (~two thirds of use) as BVd in the second line. However, the Committee considered it clinically appropriate for clinicians to have the option to use either BPd or BVd.

11.27. Members considered that people who would currently receive Pd rather than PVd at second-line (mainly due to neuropathy) would receive belantamab mafodotin as BPd if it was available, still avoiding bortezomib.

11.28. The Committee considered it reasonable to assume that uptake of belantamab mafodotin at second-line would be very high (in the absence of daratumumab being funded for second-line RRMM), despite the known ocular toxicity. The Committee considered that refinement over time of the minimum effective dose and extended dosing intervals to manage this toxicity would mean that belantamab mafodotin would likely remain the preferred second-line option. However, Members considered that third-line use of belantamab mafodotin might be considered for patients with individual reasons or due to geographic location (and consequently, access to ocular assessment).

11.29. The Committee considered that if belantamab mofodotin were used at third line, its use would mostly be in the BPd regimen because the majority of this group of people would have received bortezomib in the second line.

11.30. The Committee considered that belantamab mafodotin would displace Pd, PVd and cyclophosphamide regimens, and potentially extend the duration of some bortezomib use. Members considered that the best and most relevant available evidence for the

New Zealand current treatment at second line is PVd from DREAMM-8, which is more relevant than PVd (or Vd) data from OPTIMISMM or outcomes with Vd from CASTOR (which was less relevant given patients were less heavily pre-treated).

11.31. Members noted that unadjusted indirect comparisons would be required across multiple trials and considered that the following would be a reasonable approach to evidence for the economic analysis:

11.31.1. DREAMM-7 was likely to represent the intervention arm evidence for approximately two thirds of the group (BVd)

11.31.2. DREAMM-8 would represent the intervention arm evidence for the approximately one third of the group receiving BPd.

11.31.3. PVd from DREAMM-8 (preferred) or OPTIMISMM would be expected to represent the comparator arm evidence for the proportion who could receive bortezomib

11.31.4. Existing modelling for pomalidomide as Pd would be used to represent Pd efficacy, noting the low quality of evidence for Pd in this indication.

11.32. Members considered it reasonable to assume that the Kaplan-Meier curves for OS can be extrapolated from DREAMM-8 despite the median number of events not being reached at the time of the updated report and considered that the DREAMM-8 hazard ratio for OS was likely applicable when comparing BPd to PVd. Members noted that similar OS was reported at 12 months in DREAMM-7 (DVd control arm) and DREAMM-8 (PVd control arm) in daratumumab-exposed populations, with the curves indicating a maintained difference. Members further noted that complete response (CR) rates were high and considered that those in CR would remain on low-dose maintenance until progression. Members considered that further examination of the evidence could be undertaken to identify possible reasons for the reported difference in OS outcomes and their significance between DREAMM-7 and -8 given that both trials had reported a PFS benefit of similar magnitude.

11.33. The Committee considered that it would be expected to reduce second transplants in those who receive BPd given MRD rates are high with BPd (~25%), although noted that second transplants are only undertaken in a small proportion of patients. The Committee considered that belantamab mafodotin might also reduce the need for privately funded CAR-T cell treatments administered overseas.

11.34. Members considered that PFS is a poor surrogate for health-related quality of life in multiple myeloma, given that what constitutes progression can be highly variable (eg an asymptomatic blood test result compared with a bone fracture event), although acknowledged that prolonged PFS may avoid or delay subsequent therapy until progression.

Funding criteria

11.35. The Committee considered it reasonable for the funding criteria for belantamab mafodotin to allow access in the second or later line setting by targeting those who have received at least one prior line of therapy for multiple myeloma.

Summary for assessment

11.36. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for belantamab mafodotin if it were to be funded in New Zealand for RRMM. 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	People with relapsed or refractory multiple myeloma (RRMM) who have received at least one prior line of treatment.
Intervention	BVd - belantamab mafodotin with bortezomib and dexamethasone (approximately two thirds of use) OR BPd - belantamab mafodotin with pomalidomide and dexamethasone (approximately one third of use)
Comparator(s)	PVd – pomalidomide, bortezomib, and dexamethasone (approximately 70% of use, representing the proportion of people still able to use bortezomib without intolerable neuropathy at this treatment line) OR Pd – pomalidomide and dexamethasone (preferred for patients experiencing neuropathy)
Outcome(s)	Key outcomes: • Delayed next treatment, as represented by prolonged PFS • HRQoL to be modelled by treatment using trial data, not using PFS as a surrogate • Overall survival Key trial data to inform all key outcomes: DREAMM-8 trial to represent efficacy of BPd and PVd DREAMM-7 trial to represent efficacy of BVd.
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. Neoadjuvant nivolumab (with chemotherapy) for resectable non-small cell lung cancer (stage IB, II, or IIIA)

Application

12.1. The Committee reviewed the application for neoadjuvant nivolumab for the treatment of resectable non-small cell lung cancer.

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 nivolumab be widened to the neoadjuvant setting for people with resectable non-small cell lung cancer with a **high priority**, subject to the following Special Authority criteria:

> Nivolumab (resectable non-small cell lung cancer)
> **Initial application** – Applications only from a relevant specialist or any relevant practitioner on the recommendation of a relevant specialist. Approvals valid for 4 months for applications meeting the following criteria:
> All of the following:
> 1. Individual has resectable non-small cell lung cancer with tumour(s) ≥4 cm or node positive; and
> 2. Treatment must be prior to surgical resection (neoadjuvant treatment); and
> 3. Person has ECOG performance status 0-1; and
> 4. The treatment must be in combination with platinum-based chemotherapy; and
> 5. Neoadjuvant treatment with nivolumab is not to exceed a total of 3 doses.

12.4. In making this recommendation, the Committee considered:

12.4.1. The significant and clinically meaningful improvement in 5-year overall survival gained from neoadjuvant nivolumab plus chemotherapy compared to other perioperative approaches.

12.4.2. More effective treatments would spare a greater proportion of people from progressing and requiring subsequent treatment.

12.4.3. The proposed regimen was fixed at three cycles, which represents a potentially more resource efficient approach compared to other immunotherapy regimens.

12.4.4. Non-small cell lung cancer disproportionally impacts Māori and Pacific peoples.

Discussion

Māori impact

12.5. The Committee discussed the impact of funding neoadjuvant nivolumab for the treatment of non-small cell lung cancer (NSCLC) on Māori health outcomes and noted that the treatment of lung cancer is one of the five Māori health areas of focus | Hauora Arotahi. The Committee noted Māori are often diagnosed with more advanced disease, and that it was likely a larger proportion of Māori would not be eligible for a neoadjuvant regimen compared to non-Māori. The Committee noted the disproportionately greater incidence and mortality rates of lung cancer among Māori (Te Whatu Ora | Health New Zealand. Cancer Data Web Tool) and considered neoadjuvant nivolumab would offer a meaningful benefit to Māori.

Populations with high health needs

12.6. The Committee discussed the health need(s) of NSCLC 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 considered the impact of this funding proposal within this context and noted:

12.6.1. Māori and Pacific peoples are disproportionately affected by lung cancer, with age-standardised incidence rates of 72.19 and 42.56 per 100,000 population, respectively, compared with 23.15 per 100,000 among European/other populations between 2018–2022 (Te Whatu Ora | Health New Zealand. Cancer Data Web Tool).

12.6.2. Māori experience a lower curative resection rate (13.4%) compared to Europeans (17.2%) (Te Aho O Te Kahu | Cancer Control Agency. 2021. Lung Cancer Quality Improvement Monitoring Report).

12.6.3. Māori experience the highest mortality rates associated with lung cancer in New Zealand (Te Whatu Ora | Health New Zealand. Cancer Data Web Tool).

12.6.4. Socioeconomic status is associated with increased lung cancer incidence and mortality (Cancer Control Agency | Te Aho O Te Kahu. 2020. The State of Cancer In New Zealand).

12.6.5. The well-established association between smoking and lung cancer. The Committee noted that smoking prevalence remains higher among Māori and Pacific peoples compared to people of European descent (Te Whatu Ora | Health New Zealand. 2023/2024. New Zealand Health Survey).

Background

12.7. The Committee noted the supplier application requests widened access to nivolumab for use in the neoadjuvant setting for people with resectable NSCLC. The Committee noted the claims in this application align with the main goals of the New Zealand Cancer Action Plan 2019-2029.

12.8. The Committee considered there to be increasing attention in the clinical community to adjuvant, neoadjuvant, and perioperative treatment strategies for resectable NSCLC.

12.9. The Committee noted its previous reviews in this therapeutic setting, including:

12.9.1. An application for atezolizumab (adjuvant) for PD-L1 positive NSCLC (link to application tracker)

12.9.2. An application for Osimertinib (adjuvant) for EGFR positive NSCLC (link to application tracker)

12.10. The Committee noted Pharmac had received an application for alectinib (adjuvant) for ALK positive NSCLC, which will be considered at a future meeting (link to application tracker).

12.11. The Committee noted a letter in support of this application submitted on behalf of the Lung Oncology Special Interest Group (LOSIG), which are a group of clinicians.

12.12. The Committee noted that nivolumab is Medsafe approved for the requested indication (link to data sheet).

Health need

12.13. The Committee noted that the health need for people with resectable NSCLC was most recently reviewed by CTAC in October 2023 during the Committee's initial consideration of adjuvant atezolizumab.

12.14. The Committee noted lung cancer is reported to be the leading cause of cancer-related mortality in New Zealand (Te Aho O Te Kahu | Cancer Control Agency. 2025. Lung Cancer Quality Improvement Monitoring Report Update). The high risk of recurrence with NSCLC results in poor outcomes, significant morbidity, and a high mortality rate. The Committee noted 25-55% of people diagnosed with stage I-II NSCLC will die of recurrent disease (Rami-Porta et al. J Thorac Oncol. 2015;10:990-1003).

12.15. The Committee noted that while an estimated 30-50% of individuals present with resectable disease (Kris et al. Transl Lung Cancer Res. 2023;12:824-36), it is reported that 18.9% of people diagnosed with NSCLC received a surgical resection between 2019-2022 in New Zealand (Te Aho O Te Kahu. 2025).

12.16. The Committee noted that following resection, consideration of four cycles of adjuvant chemotherapy is the standard approach to treating resectable NSCLC in New Zealand. The Committee noted the decision to administer adjuvant chemotherapy is determined by disease stage and a variety of factors related to the individual (eg physical wellness, comorbidities, personal preference). The Committee noted neoadjuvant chemotherapy is uncommon in New Zealand, but considered the available evidence sufficient to indicate the associated health benefits comparable to those of adjuvant chemotherapy (NSCLC Meta-analysis Collaborative Group Lancet. 2014;383:1561-71 & Postmus et al. Ann Oncol. 2017;28:iv1-21).

12.17. The Committee noted compared to surgery alone, adding adjuvant chemotherapy is associated with a modest 5.4% increase in 5-year overall survival (OS) for people presenting with all stages of NSCLC (Pignon et al. J Clin Oncol. 2008;26:3552-3559).

12.18. The Committee considered that NSCLC places a heavy burden on the individual, as well as their careers and whānau.

Health benefit

12.19. The Committee noted the CheckMate 816 trial as key evidence, a multicentre, randomised, open-label, phase III investigation of adults with resectable Stage IB [≥4 cm] - IIIA NSCLC treated with neoadjuvant chemotherapy (3 cycles) with or without neoadjuvant nivolumab (3 cycles). The Committee noted that people with EGFR mutations, ALK alterations, or an ECOG performance status >1 were excluded. The Committee noted findings from the published pre-specified interim analysis 1 (median follow up: 29.5 months, Forde et al. N Engl J Med 2022;386:1973-85), the supplier-provided pre-specified interim analysis 2 (median follow up: 41.1 months), and the recently published pre-specified final analysis of overall survival (median follow up: 68.4 months, Forde et al. N Engl J Med. 2025;393:741-52).

12.19.1. The Committee considered the participant characteristics to be comparable between arms, specifically noting the similar proportions of disease stage and PD-L1 expression level.

12.19.2. The Committee noted the improved event-free survival (EFS) reported in the interim analysis 1 for those who received nivolumab and chemotherapy (31.6 months; 95%CI 30.2-not reached) compared to those who received chemotherapy alone (20.8 months; 95%CI 14.0-26.7). As reported in the final OS analysis, the Committee noted the significant increase in 5-year OS for those who received nivolumab with chemotherapy (65.4%) compared to those who received chemotherapy alone (55.0% - HR 0.72;95%CI 0.52-0.99, p=0.048). The Committee noted that OS was a statistically powered, pre-specified secondary endpoint that was planned to be tested hierarchically if the between-group difference in EFS was significant.

12.19.3. The Committee considered the evidence suggests that nivolumab with chemotherapy provided a significant and clinically meaningful improvement in OS compared to chemotherapy alone.

12.19.4. The Committee noted a subgroup analysis which suggested that the benefit in OS appeared to be greater for those with a higher stage of disease (Stage III vs stage Ib + II) and for those with PD-L1 expression levels ≥1%. Members noted the study was not designed to assess differences between these subgroups and considered there to be uncertainty regarding the validity of these findings.

12.19.5. The Committee noted adverse events of any cause led to treatment discontinuation in a similar proportion of each study arm. The Committee noted the occurrence of specific adverse events (eg nausea, anaemia, constipation) was broadly similar between study arms. The Committee acknowledged the general concern that neoadjuvant treatments may impede resection and noted there was a higher rate of definitive surgeries for those who received nivolumab and chemotherapy (83.2%) than for those who received chemotherapy alone (75.4%). There were also fewer cancelled surgeries for those who received nivolumab and chemotherapy (15.6%) than for those who received chemotherapy alone (20.7%). Overall, the Committee considered there to be comparable safety between study arms.

12.19.6. The Committee discussed the quality of CheckMate 816 trial and considered the investigation to be high quality. The Committee noted the study was open-label, lacking blinding for both participants and clinicians. The Committee noted the primary endpoints (EFS and pathological complete response) were evaluated by blinded independent central review. The Committee considered there was low risk of imprecision given the size of each study arm (n=179) and

the narrow confidence intervals observed. The Committee noted the study was industry sponsored, but generally considered the risk of bias to be low.

12.19.7. The Committee considered the evidence to be relevant and generalisable to the New Zealand context, reiterating its view that neoadjuvant and adjuvant chemotherapy are comparably efficacious. The Committee noted that the letter submitted by LOSIG also supported the use of the neoadjuvant chemotherapy arm of CheckMate 816 as an appropriate comparator to represent current practice in New Zealand.

12.20. The Committee noted that the study population (Stage IB [≥4 cm] – Stage IIIA NSCLC) was defined according to the IASLC 7th edition staging groups of the TNM Classification of Lung Cancer. The Committee noted that this population includes individuals with tumours 4 cm or larger, as well as those with tumours of any size accompanied by positive lymph nodes (including up to N2b involvement), provided the disease remains amenable to surgical resection.

12.21. The Committee considered that implementing neoadjuvant nivolumab would require a major shift in the currently utilised pathways and models of care to enable delivery of this intervention. The Committee noted this approach would depend on early multidisciplinary meeting (MDM) review, timely referral following MDM to access medical oncology first specialist assessment (FSA) and treatment, prioritisation according to clinical urgency, and referral back to surgical services for timely surgery.

12.21.1. The Committee noted the letter submitted by LOSIG which provided clinical input, and discussed the requirement for alterations of current referral and treatment pathways and agreed that prompt access to medical oncology FSA and infusion services would be critical to prevent treatment delays for people with a potentially curable disease. The Committee noted that LOSIG stated that, with appropriate resource utilisation and a coordinated effort, these alterations to the current paradigm could be implemented and sustained in New Zealand, which the Committee considered to be reasonable.

12.22. The Committee noted the following reports of real-world evidence and considered them to support the findings of CheckMate 816

12.22.1. Brunelli et al. Clin Lung Canc. 2025;26:253-261

12.22.2. Shalata et al. J Clin Med. 2025:13:6568

12.23. The Committee noted that the intention of this intervention is not to downstage advanced disease for the purpose of increasing a person's chance of becoming eligible for surgery.

Suitability

12.24. The Committee noted nivolumab is administered intravenously over 30 minutes.

Cost and savings

12.25. The Committee noted that compared to other perioperative approaches, neoadjuvant nivolumab has a fixed duration of 3 cycles and stands out as being resource efficient.

12.26. The Committee considered five-year OS as the key outcome for modelling health benefit.

12.27. The Committee noted the risk of relapse after neoadjuvant nivolumab with chemotherapy and surgical resection plateaus over time until individuals are considered cured. The Committee considered 5 years as a reasonable duration for an individual to remain in EFS before being considered cured. The Committee considered the majority of relapses occur within the first 3 years following treatment.

12.28. The Committee considered it would be reasonable to estimate the number of people eligible for treatment based on the number of surgical resections for NSCLC that occurred between 2019-2022 (Te Aho O Te Kahu. 2025). The Committee considered the 2019-2022 data to be relevant and considered there would be minimal influence from the COVID 19 pandemic. The Committee noted that the total number of resections would include people who would not be eligible for nivolumab because they had earlier stage disease (Stage IA), were not eligible for chemotherapy, or had an EGFR mutation or ALK alteration.

12.28.1. The Committee considered that the ACT-NOW database could be used to identify the proportion of people who received adjuvant chemotherapy for NSCLC.

12.28.2. The Committee considered that approximately 10% of people with NSCLC would have EGFR mutations or ALK alterations.

12.29. The Committee considered it would be reasonable to expect a greater proportion of people with resectable NSCLC to receive neoadjuvant nivolumab than are currently receiving adjuvant chemotherapy, given the favourable risk-benefit profile.

12.30. The Committee considered that very few individuals would be expected to receive adjuvant chemotherapy after having received neoadjuvant nivolumab in combination with chemotherapy. The Committee noted data from the CheckMate 816 study, which reported that 11.9% of participants treated with nivolumab plus chemotherapy subsequently received adjuvant chemotherapy after surgery, compared with 22.2% of those treated with chemotherapy alone. The Committee considered that the proportion of individuals receiving adjuvant treatment after neoadjuvant nivolumab would likely be lower than that reported in the study.

12.31. The Committee noted resection rate data from 2019-2022 which reported a 13% increase in resections over three years compared to previous reporting from 2015-2018 (Te Aho O Te Kahu. 2025). The Committee noted that this equated to 4% annual increase in resection numbers. The Committee considered this annual increase to be reasonable, particularly in light of the anticipated expansion of lung cancer screening. The Committee noted that increased targeted screening could alter the treatment landscape regarding the relative proportion of disease stage; however, it emphasised that this remains highly uncertain, given that expanding screening programmes are currently in pilot/research phase and subject to other limiting factors, such as the availability of thoracic surgeons.

12.32. The Committee considered less than 5% of people are currently receiving neoadjuvant chemotherapy.

12.33. The Committee considered the following to be reasonable estimates of medical resource use:

12.33.1. If the individual remains event-free after treatment, they would require 1 post-op visit with the surgeon; an oncology or respiratory follow up approximately every 3-6 months in year 1, then 6 monthly in years 2-5; CT imaging approximately 2–4 times in year 1, then 6 monthly in years 2 and 3, and annually in years 4 and 5; MRI and PET scans are not routinely indicated; ECGs as needed. If an individual remained event free for five years and therefore considered cured, they would no longer require medical resources associated with NSCLC.

12.33.2. For an individual with a locoregional recurrence managed with combined chemotherapy and radiotherapy, the Committee considered that a typical course of chemoradiation would involve approximately one medical oncology first specialist assessment (FSA), one radiation oncology FSA, two medical

oncology assessment visits, between two and six chemotherapy administration visits, and a six-week course of radiation therapy delivered five days per week. An oncologist visit would thereafter be required every 1-2 months for the duration of treatment if an individual received durvalumab. Approximately four CT scans would be required after treatment. This estimate does not include the diagnostic work-up, which would usually involve repeat tissue sampling (for example, CT-guided biopsy or bronchoscopy).

12.33.3. If an individual were to progress with distant metastases, they would require an oncologist visit every 3-6 weeks and would likely require approximately four CT scans and 1-2 MRIs.

12.33.4. An individual would visit the surgeon post-resection irrespective of progression.

12.34. The Committee noted that a small proportion of participants in CheckMate 816 who received nivolumab with chemotherapy went on to receive subsequent treatment, including immunotherapies such as pembrolizumab. The Committee noted that evidence is limited to support IO retreatment in advanced NSCLC following neoadjuvant therapy; however, it recognised there will be a clinical desire to allow retreatment in advanced NSCLC where disease progression occurs outside the expected window of neoadjuvant-therapy response. The Committee also noted that current pembrolizumab Special Authority criteria restrict access to individuals who have never received funded immunotherapy, which would exclude those who progress following funded neoadjuvant nivolumab.

12.35. The Committee considered there would be a small group of individuals who receive adjuvant chemotherapy rather than neoadjuvant nivolumab with chemotherapy, but noted if eligible, the vast majority of people with resectable NSCLC would receive neoadjuvant nivolumab with chemotherapy.

12.36. The Committee noted that the suppliers economic model assumes that people receiving treatment with neoadjuvant nivolumab have the same health-related quality of life as the general public and considered this was not a reasonable assumption. The Committee noted the stress of diagnosis and anxiety about recurrence are likely to have a material detriment to quality of life (Jovanovski et al. Lung Cancer Manag. 2023;12:LMT60).

Funding criteria

12.37. The Committee discussed a potential restriction based on PD-L1 expression level and considered this was not advisable given the current body of evidence. The Committee noted the 5 year OS benefit was observed in the intention to treat population in CheckMate 816 (Forde et al. 2025). The Committee acknowledged the PD-L1 subgroup analysis suggesting a possibly greater treatment effect in patients with PD-L1 ≥1%, but considered that additional evidence would be required before PD-L1 expression–based criteria could be considered.

Summary for assessment

12.38. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for neoadjuvant nivolumab if it were to be funded in New Zealand for resectable non-small cell lung cancer. 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	Adults with resectable Stage IB (≥4 cm) - IIIA non-small cell lung cancer (NSCLC) who are considered eligible for chemotherapy. Patients must have an ECOG score of 0 – 1 and not have either EGFR mutation or ALK rearranged disease.
Intervention	Neoadjuvant nivolumab (360mg once every 3 weeks for 3 cycles) PLUS Neoadjuvant chemotherapy once every 3 weeks for 3 cycles
Comparator(s)	Surgical resection followed by chemotherapy once every 3 weeks for 4 cycles
Outcome(s)	Increased overall survival and time spent in EFS
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.	