BCAC Submission to Pharmac for OLAPARIB

Overview

A separate clinical summary is provided. The submission concerns 2 indications:

- For early breast cancer
- For metastatic breast cancer

Product Details

What is the registered name of the generic pharmaceutical?

olaparib

What is the brand name of the pharmaceutical?

LYNPARZA®

Which therapeutic area does this pharmaceutical fall into?

Oncology

Please provide information on the various forms, strengths, and pack sizes of the pharmaceutical that you are seeking funding for.

100mg tablets 56 tablet pack

150mg tablets 56 tablet pack

Which companies produce and/or supply the pharmaceutical?

AstraZeneca

Proposed amendments

As monotherapy or in combination with endocrine therapy for the adjuvant treatment of adult patients with germline BRCA1/2-mutations who have HER2-negative, high risk early breast cancer previously treated with neoadjuvant or adjuvant chemotherapy.

As monotherapy for the treatment of adult patients with germline BRCA-mutated HER2 negative metastatic breast cancer.

Disease and Current Treatment

Please provide an overview of the disease for which funded treatment is sought.

Breast cancer is diagnosed in about 3,500 people annually in New Zealand. The latest Ministry of Health mortality report shows nearly 700 deaths in 2019. It is therefore an important health issue in terms of physical and mental health and has a significant social and economic impact on society, families, and whānau. Despite the perception that cancer is an older person's disease, breast cancer is the number one cause of death for New Zealand women under 65. Having a relative living with or dying of breast cancer affects other family members significantly.

A report by the New Zealand Breast Cancer Foundation in 2018 found that median survival after a diagnosis of metastatic/advanced breast cancer in New Zealand is 16 months, considerably worse than overseas. For example, this compares with 29.4 months in the Netherlands, 36.8 months in Germany, 25 - 54 months in the USA, 23.1 months in France, and 33 months in Sweden. Therefore,

although there have been improvements in rates of survival for breast cancer over the past decades, New Zealand still lags behind equivalent countries, for survival of people with metastatic breast cancer (Breast Cancer Foundation New Zealand 2018).

Breast cancer treatment is individualised based on tumour characteristics, patient characteristics and treatment history. Approximately 5% of unselected patients with breast cancer carry a germline BRCA mutation. Such mutations are more likely to be present in patients who have a strong family history of breast cancer, younger patients, patients who have triple-negative breast cancer, and patients who are members of an ethnic group with known founder mutations in the BRCA genes.

Patients with a BRCA1 mutation are predisposed to triple-negative breast cancer, whereas patients with a BRCA2 mutation most often have tumours that express oestrogen receptors. BRCA1 and BRCA2 are tumour-suppressor genes that encode proteins involved in the repair of DNA double-strand breaks by way of the homologous recombination repair pathway (Robson, Im et al. 2017).

An updated ASCO guideline for Endocrine Treatment and Targeted Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer BRCA1 or BRCA2 mutation carriers with metastatic HER2-negative breast cancer, olaparib or talazoparib should be offered in the 1st-line through 3rd-line setting (Burstein, Somerfield et al. 2021).

ESMO guidelines (2021) state that olaparib (or talazoparib) should be considered for patients with ER+/HER- germline pathogenic BRCA1/2 mutations [I, A; ESMO-MCBS v1.1 score: 4; ESCAT score: I-A] and as an option for those with somatic pathogenic or likely pathogenic BRCA1/2 or germline PALB2 mutations, as shown below (Figure 2 from the 2021 ESMO Guidelines).

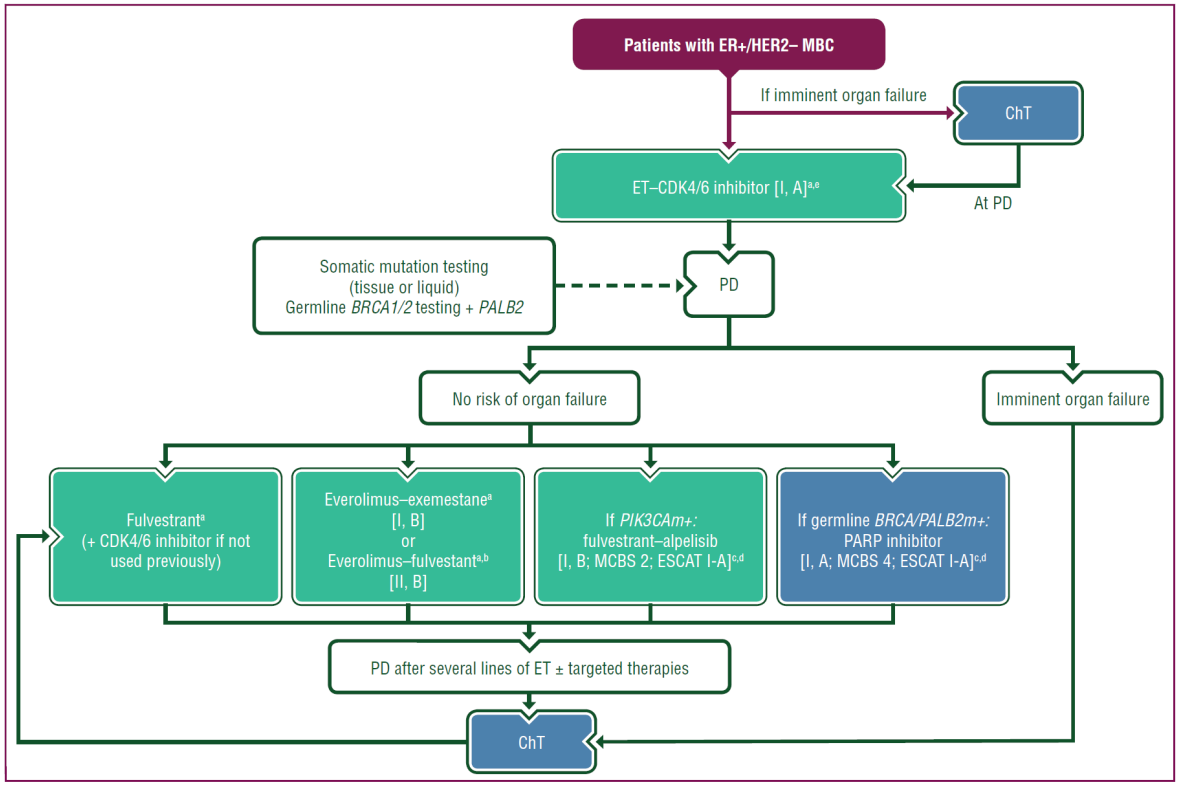


Figure 2. Treatment of ER-positive/HER2-negative MBC.
Purple: general categories or stratification; turquoise: combination of treatments or other systemic treatments; white: other aspects of management; blue: systemic anticancer therapy.
AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4 and 6; ChT, chemotherapy; EMA, European Medicines Agency; ER, estrogen receptor; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; ESR1, estrogen receptor 1; ET, endocrine therapy; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; m, mutation; MBC, metastatic breast cancer; MCBS, ESMO-Magnitude of Clinical Benefit Scale; OFS, ovarian function suppression; *PALB2, partner and localiser of BRCA2*; PARP, poly (ADP-ribose) polymerase; PD, progressive disease; *PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha*.
[a] OFS if the patient is premenopausal.
[b] Preferred if the patient is *ESR1* mutation positive [ESCAT score: II-A].[d]
[c] ESMO-MCBS v1.1[93] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1/scale-evaluation-forms-v1.1).
[d] ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[89]
[e] If relapse <12 months after end of adjuvant AI: fulvestrant—CDK4/6 inhibitor[a]; if relapse >12 months after end of adjuvant AI: AI—CDK4/6 inhibitor[a].

Source: (Gennari, André et al. 2021)

ESMO guidelines also recommend the use of olaparib for patients with triple negative breast cancer who are germline BRCA positive (Figure 5 below). Two randomised studies of patients with HER2-negative MBC and gBRCAm previously treated with anthracyclines and/or taxanes demonstrated that treatment with a PARP inhibitor (olaparib, talazoparib) resulted in statistically significant improvements in PFS compared with capecitabine, vinorelbine, eribulin or (in one study) gemcitabine. OS was not improved but a post hoc subset analysis of one study suggested improved OS in patients receiving olaparib who had not received prior ChT for metastatic disease. Notably, over 40% of the control arm in each study received a platinum or PARP inhibitor after progression on study treatment (Gennari, André et al. 2021).

The patients enrolled in the pivotal trials were largely women. However, there is no plausible biological reason to expect lower efficacy in men with MBC and gBRCAm. Eligibility criteria for the studies included prior treatment with (or inappropriateness for) anthracycline taxane ChT. This selection was guided by regulatory considerations rather than a biological rationale. Therefore, PARP inhibitors should not be withheld from patients without prior anthracycline taxane treatment. Indeed, based on the subset analysis of OlympiAD, requiring progression on these agents in the metastatic setting may be associated with a lower magnitude of OS benefit. Patients with HR-

positive MBC and gBRCAm do benefit from PARP inhibitor treatment, with no statistical evidence of heterogeneity of effect in either of the pivotal phase III trials (Gennari, André et al. 2021).

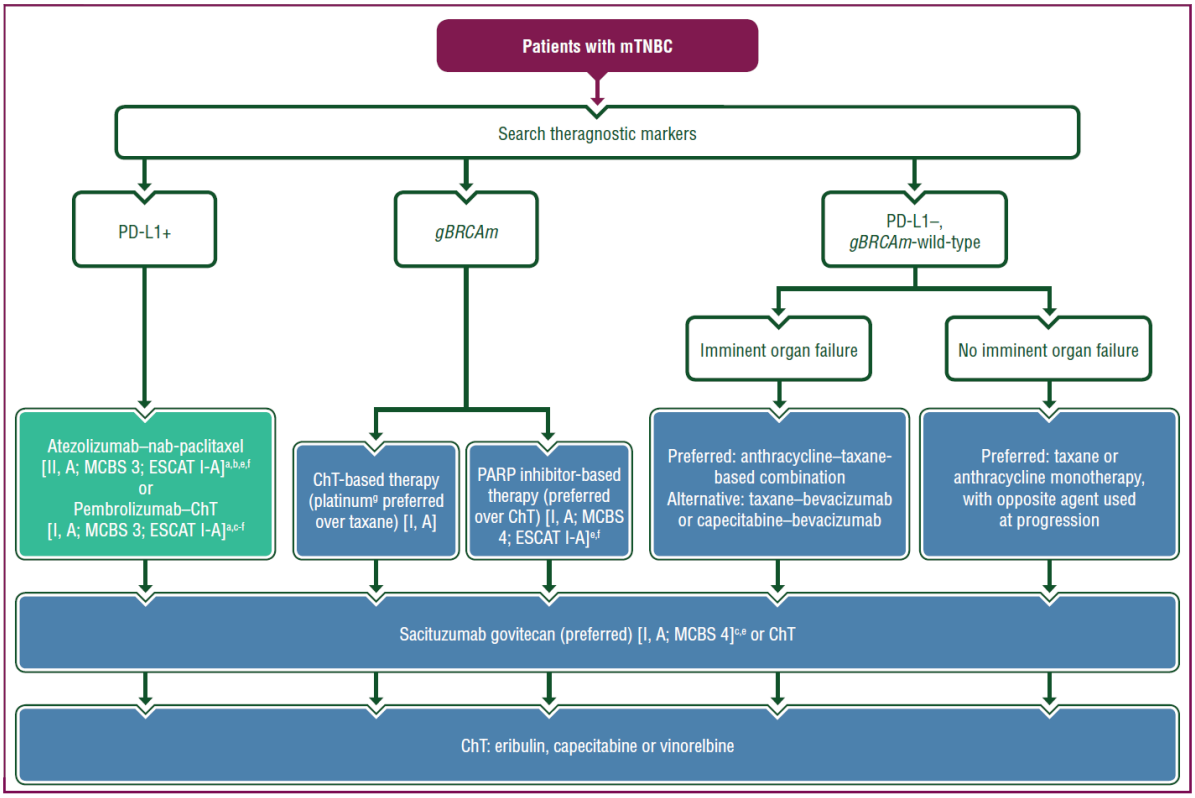


Figure 5. Treatment of mTNBC.
Purple: general categories or stratification; turquoise: combination of treatments or other systemic treatments; white: other aspects of management; blue: systemic anticancer therapy.
ChT, chemotherapy; EMA, European Medicines Agency; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; FDA, Food and Drug Administration; *gBRCAm*, germline *BRCA1/2* mutation; ICI, immune checkpoint inhibitor; MCBS, ESMO-Magnitude of Clinical Benefit Scale; mTNBC, metastatic triple-negative breast cancer; PARP, poly (ADP-ribose) polymerase; PD-L1, programmed death-ligand 1.
[a] May be considered as monotherapy in further lines in case of high PD-L1 positivity and no previous exposure to ICI.
[b] EMA approved, not FDA approved.
[c] FDA approved, not EMA approved.
[d] ChT physician's choice of nab-paclitaxel, paclitaxel or gemcitabine/carboplatin.
[e] ESMO-MCBS v1.1[93] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1/scale-evaluation-forms-v1.1).
[f] ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[89]
[g] If not used previously.

Source:(Gennari, André et al. 2021)

BCAC and its member groups are justifiably concerned about the poor access to treatments in New Zealand for people with BRCA germline mutation breast cancer. It is particularly important that treatments that are already recommended by clear-cut consensus within the breast cancer community are subsidised so that all those with breast cancer can access them, irrespective of their ability to pay.

Does the disease impact on the health of the patient's family, whānau or wider society? Please explain and provide sources of information.

Breast cancer is diagnosed in about 3,500 people annually in New Zealand. The latest Ministry of Health mortality report shows nearly 700 deaths in 2019. It is therefore an important health issue in terms of physical and mental health and has a significant social and economic impact on society,

families, and whānau. Despite the perception that cancer is an older person's disease, breast cancer is the number one cause of death for New Zealand women under 65.

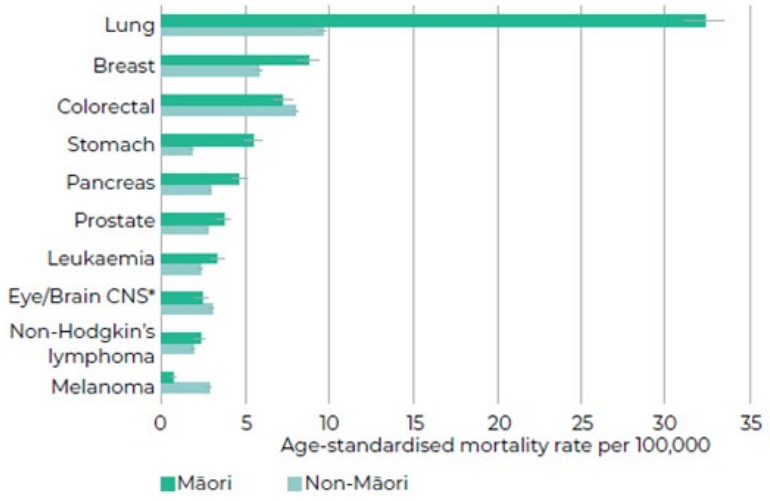
Women undertake many vital roles in our society, both professional and unpaid. These include caring for elderly parents, children and other family members, keeping households fed and running effectively and providing emotional support for friends and whānau. Keeping women alive with a good quality of life has huge benefits for families and society.

What is the impact of the disease on Māori health outcomes? Please explain and provide sources of information.

In recent years, approximately 3,500 have been diagnosed with breast cancer annually in Aotearoa New Zealand; this number has steadily increased over time in line with our growing and aging population. The actual rate of diagnoses (per 100,000 women) has increased slightly over the past 20 years for both wāhine Māori and non-Māori women (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021). In 2018, the incidence of breast cancer per 100,000 women was 124.9 for Māori and 97.4 for non-Māori (Ministry of Health 2020). It is therefore of significant concern that Māori health outcomes, particularly for wāhine Māori are being impacted by poor access to treatments for breast cancer.

Wāhine Māori are more likely to be diagnosed with advanced disease and are more likely to die from breast cancer than non-Māori/non-Pacific women. Pacific women are also more likely to be diagnosed with advanced disease and more likely to die of breast cancer than non-Māori/non-Pacific women.

Age- and sex-standardised cancer-related mortality 2007–2017



* CNS = central nervous system

Source: (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021)

Does the disease fall into one of the categories of PHARMAC's Māori health areas of focus?

Yes

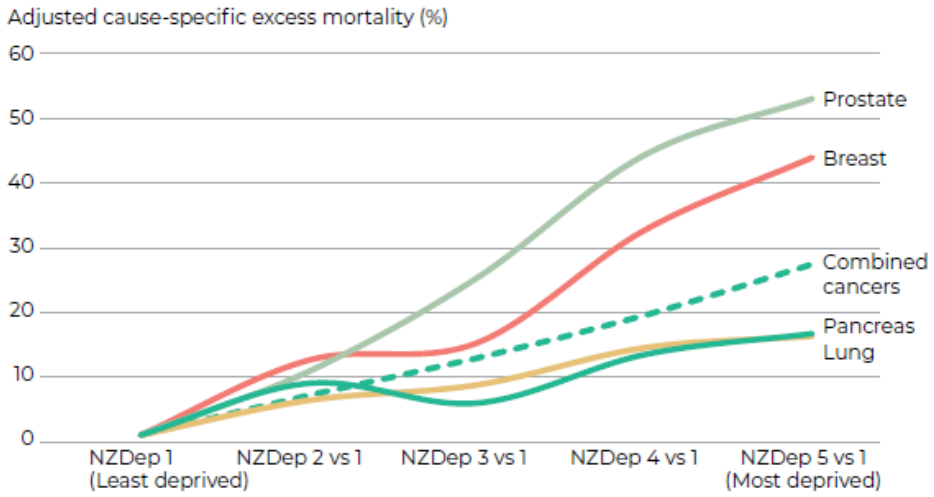
Does the disease disproportionately affect population groups that may already be experiencing a health disparity?

People who are economically deprived are already in poorer health in New Zealand. Overall, cancer incidence is higher among those living in the more deprived areas – although this varies depending

on the type of cancer. Poverty is a barrier to accessing early diagnosis and best-practice treatment for cancers, leading to inequities in cancer survival between the poor and the affluent. This is particularly important for highly treatable cancers, where finding a cancer early and treating it quickly can significantly improve survival outcomes (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021).

The figure below (from Te Aho), shows the impact of economic deprivation on survival

Impact of deprivation on cancer survival, 2007–2016



Source: (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021)

The fact that many New Zealanders must personally pay to gain access to cancer medicines that are evidence-based and recommended by their oncologists is creating a two-tiered health system in which those who can pay will live longer. Families are being forced to cash in retirement savings, sell properties, set up 'Give a Little' pages and fundraise to gain benefits in quality of life, progression free survival and overall survival. This situation is lamentable and does not contribute to the notion of equity within health care. The Ministry of Health's definition of equity is: "In Aotearoa New Zealand, people have differences in health that are not only avoidable but unfair and unjust. Equity recognises different people with different levels of advantage require different approaches and resources to get equitable health outcomes."

People living with mental health and addiction issues have significantly reduced life expectancy compared with the general population, mainly due to dying early from physical illnesses, such as heart disease and cancers. Access to and quality of health care are major contributors, including access to cancer screening, timely diagnosis, and treatment. Research in Aotearoa has found that, among people diagnosed with breast or colorectal cancers, survival is much poorer for those with a history of recent contact with specialist mental health services (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021).

Who is the target population?

Patients with germline BRCA mutation positive breast cancer

Costs

Please detail whether there are any additional health-related costs or savings to the person receiving treatment that are likely to be incurred if the pharmaceutical is funded.

This is an oral treatment and therefore patients would have minimal additional costs associated with treatment.

Please detail whether there are any health-related costs or savings that may be experienced by the family, whānau and wider society of the person receiving the treatment, if the pharmaceutical is funded.

The treatment related costs to family/whanau are reductions in expenditure compared with the current situation. For society as a whole, access will be available to more individuals - including those who are currently more economically disadvantaged, therefore there will be an incremental cost associated with making this treatment available on the Pharmaceutical Schedule. From a societal perspective, the cost per patient will be considerably less as Pharmac should be able to achieve a more favourable (rebated) price than patients are currently paying. Plus, the additional costs associated with treatment such as GST, administration costs (which are at a premium in the private sector) and costs to attend private clinics will be shifted from being a patient responsibility, to being borne by the public health system.

Suitability

Are there any features of the pharmaceutical that may impact use by the person receiving the treatment? If so, please explain.

This is an orally administered treatment and is therefore very convenient for patients to self administer at home. This will reduce the costs associated with attending hospital outpatient clinics. It will also reduce current costs to patients or whanau who are paying for their own therapy.

References

Breast Cancer Foundation New Zealand (2018). "I'm still here" Insights into living – and dying – with Advanced Breast Cancer in New Zealand.

Burstein, H. J., M. R. Somerfield, D. L. Barton, A. Dorris, L. J. Fallowfield, D. Jain, S. R. D. Johnston, L. A. Korde, J. K. Litton, E. R. Macrae, L. L. Peterson, P. Vikas, R. L. Yung and H. S. Rugo (2021). "Endocrine Treatment and Targeted Therapy for Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer: ASCO Guideline Update." J Clin Oncol **39**(35): 3959-3977.

Gennari, A., F. André, C. H. Barrios, J. Cortés, E. de Azambuja, A. DeMichele, R. Dent, D. Fenlon, J. Gligorov, S. A. Hurvitz, S. A. Im, D. Krug, W. G. Kunz, S. Loi, F. Penault-Llorca, J. Ricke, M. Robson, H. S. Rugo, C. Saura, P. Schmid, C. F. Singer, T. Spanic, S. M. Tolaney, N. C. Turner, G. Curigliano, S. Loibl, S. Paluch-Shimon and N. Harbeck (2021). "ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer[☆]." Annals of Oncology **32**(12): 1475-1495.

Ministry of Health (2020). New Cancer Registrations.

Robson, M., S. A. Im, E. Senkus, B. Xu, S. M. Domchek, N. Masuda, S. Delaloge, W. Li, N. Tung, A. Armstrong, W. Wu, C. Goessl, S. Runswick and P. Conte (2017). "Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation." N Engl J Med **377**(6): 523-533.

Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa (2021). The State of Cancer in New Zealand 2020.