bcac breast cancer aotearoa coalition

Together we're stronger

Tangata tū pakari tonu

Jared Solloway,

Therapeutic Group Manager – Oncology

Pharmac

Wellington

Dear Jared,

The Breast Cancer Aotearoa (BCAC) is a patient-based charity and incorporated society run by New Zealand women who have experienced breast cancer, both early and advanced. We support, inform and represent those diagnosed in Aotearoa from an evidence basis. BCAC has over 30 member groups as well as individual members from across the country.

In August 2022, we applied to Pharmac to have eribulin added to the Pharmaceutical Schedule for those with locally advanced or metastatic breast cancer who have had prior therapy for advanced or metastatic breast cancer. In doing so, we were responding to needs expressed by patients in New Zealand who are already receiving treatment and those who have had this treatment suggested to them by their oncologists but cannot afford to pay for it.

We have subsequently received the minutes of the PTAC meeting of November 2022 in which we note our application was recommended for decline. Here we respond to PTAC's decline recommendation.

We request that our submission now be referred to Pharmac's Cancer Treatments Advisory Committee (CTAC) for consideration. We would welcome the opportunity to meet with PTAC representatives or Chair to discuss our eribulin application.

PTAC Comment	BCAC Response
Recommendation The Committee recommended that eribulin for the treatment of locally advanced or metastatic breast cancer that has progressed following two prior lines of chemotherapy be declined. In making this recommendation, the Committee noted: 1.4.1. the significant health need of people with advanced or metastatic breast cancer, particularly for Māori and Pacific peoples; 1.4.2. that the evidence was conflicting and of low quality and that the results were not generalisable to the New Zealand population demographic; 1.4.3. the less-favourable adverse event profile for eribulin; 1.4.4. the minimal evidence of benefit from eribulin for the requested population.	BCAC is extremely disappointed in this recommendation and the stated reasons underpinning it. We have significant concerns about issues raised in the PTAC minutes. We also question why this submission was not sent to CTAC for its expert review. It is difficult to follow the logic of the significant health need in Māori and Pacific women being used as a reason for this recommendation to decline listing of eribulin. Surely the significant health need would support the rationale for a recommendation to list with priority, not decline. We assert that eribulin would help address the significant health needs in these populations as well as for all women with advanced breast cancer in New Zealand. BCAC does not agree the evidence is conflicting and of low quality – indeed this summary is <u>not supported by what is stated in the PTAC minutes</u>. This statement is not only inaccurate but also inconsistent with the clinical trial results summarised in the minutes. BCAC does not agree that results of the clinical trials are not generalisable to the New Zealand population. PTAC provides no plausible explanation for why they have this opinion. This issue is addressed further below. The statement that eribulin has a "less-favourable adverse event" profile lacks clarity as it does not state with what it is being compared. This hanging comparative is vague, lacking in evidence and inconsistent with trial results summarising adverse events, discontinuation, side effects, quality of life and tolerability in the minutes. This issue is addressed further below. Lastly, the statement that there is minimal evidence of benefit for the requested population is simply inexplicable when one considers that it is registered in over 70 countries for this indication. It is recommended in all key guidelines (such as ESMO, NCCN and NICE) for treatment of advanced breast cancer. Most recently and importantly it is recommended in the NZ Guidelines for ABC, published in 2022 (Breast Cancer Special Interest Group (Breast SIG) New Zealand 2022). This issue is addressed further below.
1.9 The Committee noted that approximately 5.8% of wāhine Māori living with breast cancer are diagnosed at an advanced or metastatic stage, compared to 4.7% of those of	The two reports are based on the NZ Breast Foundation Breast Cancer Register. The report entitled "I'm Still Here" is based on the period 2000-2015 and includes patients in Auckland, Waikato, Wellington and Christchurch, being 70% of the country in terms of population (Breast Cancer Foundation New Zealand 2018). As for representativeness of the people on the register in these areas, compared with the entire population, these patients might well have had better outcomes than the entire population (not worse) as they are all areas with access to specialist cancer

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European ethnicity (Breast Cancer Foundation National Register 2003-2020 report). The Committee noted that the proportion of Pacific women diagnosed at an advanced or metastatic stage is even higher, at 10.2%. The Committee noted, however, that the referenced Breast Cancer Foundation report did not have complete national data for the time period reported, thus the true epidemiology of advanced breast cancer is New Zealand may be slightly different to what is reported.	services. Therefore, the NZBCF report may well overestimate survival in the NZ population of women with advanced breast cancer, rather than underestimate it. Also it should be noted that since 2020, the entire population is included in the NZ BC Register.
1.16 The Committee noted that the manufacturer and supplier of eribulin was heavily involved in all stages of the EMBRACE, Study 301, and Yuan et al. trials and considered this cast significant uncertainty over the validity of the results reported from these trials. The Committee considered that, in general, the evidence for benefit of eribulin in locally advanced or metastatic breast cancer was of average strength and quality. The Committee also considered that the studies were not generalisable to the New Zealand	The observation that the manufacturer's sponsorship invalidates evidence from trials seems to imply that registration trial results are suspect because they have a sponsor. The PTAC provides minimal objective evaluation of the validity of the trials themselves, which should be evaluated objectively irrespective of who has sponsored them. We note that the Tanni et al. (2021) meta-analysis did evaluate the individual trials for systematic bias (Figure 2) and considered most clinical trials to have a low risk of bias. Study 301 was assessed by the American Society of Clinical Oncology (ASCO) in determining guidelines for treatment of patients with advanced breast cancer and was given a GRADE Score of Moderate. Results from Study 305 (EMBRACE) were given an ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) score of 2. The pooled analysis reported by Pivot et al. was given an EMSO-MCBS score of 1. This sort of blanket dismissal of results from "sponsored" trials would result in a lack of regulatory approval for nearly every medicine currently registered in New Zealand as well as most of those that are currently funded on the Pharmaceutical Schedule. It is unacceptable that the PTAC provides no evidence for their assertion that the evidence of benefit is "of average strength and quality". Also, this is inconsistent with the statement supporting the recommendation to decline that the evidence was of low quality. We do not believe that PTAC's process has evaluated all the relevant evidence in a fair and unbiased way.

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population, as the vast majority of participants in the trial were Caucasian.	There is ample evidence of the benefit of eribulin versus other active chemotherapies. Its effect on overall survival and other patient relevant outcomes versus other active agents was ably demonstrated in our submission. For example, the systematic review and meta-analysis by Tanni et al. concluded that eribulin has a manageable toxicity profile and provides significant survival benefit in LABC/MBC patients (Tanni, Truong et al. 2021). Subgroup analyses show that it is particularly suitable for treatment of women with MBC who are HER-2 receptor negative including those who have TNBC (Cortes, O'Shaughnessy et al. 2011, Tanni, Truong et al. 2021, Zhao, Hughes et al. 2021). This is direct contrast to what PTAC minutes stated about the lack of evidence in relevant sub-groups. There is now a further accumulation of evidence on the use of eribulin. There are Australian and UK studies that have recently been published that also support its use (Chan, Lomma et al. 2022, Jafri, Kristeleit et al. 2022). The comment about generalisability is simply inexplicable as most women in New Zealand with advanced breast cancer are also Caucasian and the submission also included trials carried out in Asian patients. While we share PTAC's aspiration that all medicines be trialled on a representative population, we recognise the need to be realistic and accept that such data does not currently exist. Rejection of trial results that do not incorporate our Māori and Pacific populations will clearly disadvantage these wāhine and all others in Aotearoa. The PTAC presents no evidence or even plausible argument that wāhine Māori and Pacific women (presumably the underrepresented ethnic groups in trials) would respond differently to this treatment. Indeed, should this be the case, then treatment could be restricted to exclude wāhine Māori and Pacific women from access. This would, however, be unethical and would likely infringe the human rights of these women. We have deep concerns about the opinion being expressed that treatments that have not been specifically tested in Māori and Pacific women should not be accessible to them or others, especially when these population groups are so clearly in need of better treatments. This could apply to every treatment currently funded for breast cancer in New Zealand today.
1.17 The Committee noted that international guidelines recommend eribulin in the treatment of ER+/HER2-negative and TNBC breast cancers. The Committee noted that individuals with HER2-positive breast cancer	Eribulin is indeed recommended in ESMO guidelines as stated (Gennari, André et al. 2021). It is also recommended by NICE and PBAC and other credible bodies internationally who have considered the evidence for effectiveness. More importantly, it is also recommended in the recently published New Zealand guidelines (Breast Cancer Special Interest Group (Breast SIG) New Zealand 2022). We are concerned that having one treatment option for patients is seen as the standard of practice that we should be aspiring to.

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have more options with HER-2 targeting therapies such as trastuzumab and trastuzumab-emtansine. The committee noted that ESMO guidelines (Ann Oncol 2021;32:1475-1495) for TNBC treatment includes eribulin as a third line of treatment option. The Committee noted that in New Zealand there is at least one funded option in each treatment arm of the ESMO guidelines.	Patients are individual in their characteristics and the treatment choices may differ from one to another. This is out of step with international and local recommendations and does nothing to address current treatment outcomes. It is not clear what is meant by the statement that there is at least one funded option in each treatment arm of the ESMO guidelines. For TNBC, this is untrue. Indeed, the following agents included in the ESMO TNBC Guidelines' algorithm are not available reimbursed in New Zealand: atezolizumab; nab-paclitaxel; pembrolizumab; PARP inhibitors, bevacizumab and sacituzumab govitecan. Implying that New Zealand women with TNBC are well served with options with respect to the ESMO guidelines misrepresents the current state of access to recommended treatments, particularly for women with TNBC. It should be a priority to address these deficits in access to treatment with better availability of a range of treatments shown to improve outcomes.
1.18 The Committee noted that progression free survival is a measure of biological activity, and not a clinical efficacy measure. The Committee considered that people living with cancer want to achieve clinically meaningful beneficial effects on their disease related symptoms, their ability to carry out normal activities, and on their overall survival.	BCAC represents people with breast cancer including people with advanced disease. Lack of progression is of relevance to patients, as is quality of life and overall survival. All these outcomes were evaluated in eribulin trials. BCAC, as a group that represents people with breast cancer, would not have applied for this treatment if the outcomes with eribulin were irrelevant for patients with breast cancer.
1.19 The Committee considered that, overall, it is unclear if eribulin provides any additional benefit over what is currently available, and that the safety profile of eribulin is not favourable compared to available chemotherapies. The Committee noted that there was limited	This blanket statement is at odds with the summary of the clinical evidence provided in the minutes (17 cited publications, which were mostly positive). The evidence was highly supportive of the benefits of eribulin as another option for NZ women with for the treatment of locally advanced and metastatic breast cancer. The benefit of eribulin versus other active chemotherapies on overall survival was demonstrated in our submission. For example, the systematic review and meta-analysis by Tanni et al. concluded that eribulin has a manageable toxicity profile and provides significant survival benefit in LABC/MBC patients (Tanni, Truong et al. 2021). Subgroup analyses show that it is particularly suitable for treatment of women with MBC who are HER-2

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evidence for benefit for people with TNBC or HER2-negative disease specifically.	receptor negative including those who have TNBC (Cortes, O'Shaughnessy et al. 2011, Tanni, Truong et al. 2021, Zhao, Hughes et al. 2021). This is direct contrast to what PTAC states in the minutes about limited evidence in the subgroup with TNBC or HER-2 negative disease.
1.20 The Committee noted that eribulin would require compounding by a third-party compounder or within an aseptic cytotoxic compounding facility and that not all hospitals have these facilities Members considered that there may be only one hospital in the country with compounding facilities. They noted that once compounded, eribulin has a shelf life of approximately two weeks. The Committee considered that infusion with eribulin would also increase the burden on infusion centres and facilities.	All centres in New Zealand that administer chemotherapy have access to compounding facilities either in house or via a third-party provider. The statement that only one hospital in the country has compounding facilities is misleading as all hospitals administering chemotherapy have access to compounding services. Indeed, this is specifically recognised in the "ECP" price in the Pharmaceutical Schedule. This is no different from many other chemotherapeutic agents used for treatment of cancer and breast cancer. Eribulin is available as a ready to use solution which should be administered intravenously over 2-5 minutes. Alternatively, eribulin can be diluted in 100 mL of normal saline for injection. Administration time of eribulin is relatively short compared to other chemotherapy agents. Also, it has been used in home-based infusion protocols elsewhere, such as in Australia. This option would contribute to overcoming ethnic and locational inequities by make treatment available closer to whānau and at home. The point of adding a proven treatment for advanced breast cancer is to give patients longer lives of better quality. The concern about resulting burden on infusion centres and facilities suggests the additional work involved in delivering a treatment outweighs the benefits of better patient survival. This thinking will do nothing to reduce ethnic inequities in Aotearoa or the survival deficit between our country and others.
1.21 The Committee noted that treatment with eribulin would require travel to an infusion service/oncology unit and this may not be feasible for people living in areas where these services are not readily available.	This is the same for all chemotherapy. Patients would have a choice to travel or not have access to treatment. This implies that because some patients would not travel to access this treatment that all patients should be denied it! As already stated, there is the potential to administer this treatment in the home. Rural patients and those who choose to remain close to whānau during treatment could achieve this with appropriate support.
1.22 The Committee considered that the number of eligible individuals per year is likely closer to the Cancer Treatments Subcommittee (CaTSoP; now the Cancer	The annual number of patients with advanced breast cancer is around 350. As this is a third line treatment, the numbers would be much lower than this. We therefore consider this estimate of patient numbers to be a gross overestimate of the potential numbers to be treated. Eribulin is an additional line of treatment that confers additional benefits in terms of survival on the individuals being treated. This

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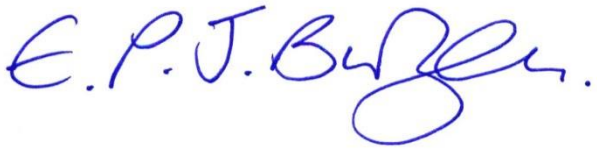
Treatments Advisory Committee)'s upper estimate of 400 (April 2019), but noted that it is unknown how many would advance to metastatic or advanced disease after their initial diagnosis of breast cancer. The Committee considered that eribulin would represent an extra line of treatment to the current treatment paradigm, therefore there would be no cost offsets.	is the objective of providing services rather than saving money by letting people die earlier without access to effective treatment. The committee makes no comment on the cost of treatment with eribulin which is considerably less than many other treatments, both current and future. There are currently patients in New Zealand paying for treatment (on recommendation of their oncologists) and this is creating the very inequities that we should be aiming to address.

We hope that the significant issues raised in this letter will prompt a reconsideration by PTAC of their recommendation and a referral to CTAC for some further advice. We look forward to your response.

Yours sincerely,



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cc. Toni Broome, PTAC Secretary