bcac breast cancer aotearoa coalition

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27 November 2024

BCAC response to Pharmac proposal to decline eribulin

Kia ora Jared, Logan and Priyanka,

We ask that Pharmac consider the new evidence and reasoning we provide to reverse its decision to decline eribulin as a treatment option for advanced breast cancer. Declining this medicine would mean that a completely new application would be required to enable a fresh perspective to be taken by Pharmac. This would condemn submitters, Pharmac staff and assessors to the complex, prolonged and time-consuming processes that constitute the application and assessment pathway. With the new data submitted here, along with a changing treatment paradigm, we ask for a more responsive and efficient approach to be taken and that our response be referred directly back to CTAC for consideration.

We note the low cost and fast infusion/injection time for this medicine. Eribulin is not a new game-changing medicine but a well-established chemotherapy agent that will provide oncologists and their patients with a much-needed alternative or additional treatment option, especially in the later line setting where there is a clear unmet health need.

Medsafe registration

Medsafe registration for eribulin was granted on 24th April 2024.

HALAVEN is indicated for the treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless these are contraindicated.

Response to PTAC decline recommendation

BCAC disagreed with many elements of PTAC's original decline recommendation. We append our original response to that decision along with a spreadsheet that shows superiority, equivalence or inferiority of trial endpoints, tolerability etc from the

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publications we cited in our application for this medicine that were summarised by PTAC. We did not find that PTAC's second consideration adequately addressed the issues raised by us in our response.

Response to elements of CTAC decline recommendation

Recommendation

1.4 The Advisory Committee recommended decline based on:

• *The uncertainty of the health benefit based on clinical trial evidence.*

There are many international examples of eribulin delivering health benefit from use as a single agent and as a partner for other treatments. In this response we provide new data on eribulin, both clinical trial results and Real World Evidence (RWE), published since PTAC first reviewed our application for eribulin in November 2022.

First registered in 2010, eribulin has been well-established for many years internationally as a safe and efficacious chemotherapy option in advanced breast cancer. The long duration of use along with evolving requirements to determine the effects of medicines on people outside the context of clinical trials has resulted in the emergence of RWE in the diverse populations treated with this medicine. The FDA now requires post-approval reporting of RWE from populations of patients being treated with medicines, confirming the importance and value of such evidence. RWE provides a genuine measure of the impacts of a medicine in the community, outside the limited groups selected for participation in clinical trials, where uniformity of participants is imposed to reduce variability in results and enable impacts to be statistically demonstrated more easily on smaller groups of patients. We ask that Pharmac consider the RWE that we present in our response as valid and useful information in assessing the safety and efficacy of eribulin.

• *Insufficient evidence to suggest benefit adding to existing treatments.*

Eribulin has been shown to be a tolerable chemotherapy option that has PFS and OS benefits across a range of indications in later line and earlier use, both as a single agent and in combination with other treatments, for a range of sub-types of advanced breast cancer across diverse populations. It continues to be used as a standard of care in multiple countries and has demonstrated efficacy and tolerability in a range of settings (please see summary of recent literature). Evidence continues to emerge for eribulin benefit in HR positive, HER2 positive, HER2-low, HER2-ultralow and TNBC. It has been shown to be equally effective as and less toxic than a taxane as a partner to a dual HER2 blockade. We note that maintaining Quality of Life is of great importance for those with advanced breast cancer and is increasingly recognised by researchers and oncologists as a significant factor in selecting treatment regimens. Eribulin can be used safely in older patients with advanced breast cancer and is suggested for earlier line use in such patients. It is also tolerable and efficacious in heavily pre-treated patients and in patients previously treated with immunotherapy or an antibody drug conjugate or a PI3K inhibitor.

Health benefit

1.11 The Committee noted that the treatment paradigm is different in New Zealand compared to internationally, with participants in trials having additional prior lines of therapy in comparison to the New Zealand population.

The treatment paradigm is changing in New Zealand as new medicines are added to the Pharmaceutical Schedule. Recent additions for advanced breast cancer include ribociclib and pembrolizumab, with trastuzumab deruxtecan to be added from 1st January 2025. Denying access to a medicine on the basis of a 'snapshot' of reduced availability at the time of a decision lacks foresight and will exclude patients from current and future treatment paradigms. Some of the new evidence on eribulin was obtained in countries with limited treatment options such as China and India.

It is unrealistic to expect New Zealand patients to have received the same set of treatments as those offered in particular overseas clinical trials. There will seldom be an RCT that perfectly mimics the treatment history of NZ patients at any given time. Such a requirement would exclude us from access to many new and older therapies. Treatment paradigms evolve overseas and in New Zealand as new medicines become available. Some flexibility is needed to allow NZ patients to access efficacious treatments that are widely available overseas. Whatever prior treatments have been administered, it is highly likely that patients with advanced breast cancer will need later line chemotherapy options after other treatments fail or have resulted in intolerable side effects. Eribulin would provide a further treatment for patients who are running out of options. Recent studies suggest a range of other indications as a less toxic partner therapy.

1.13.2 The Committee noted that the treatments received in the treatment of physician's choice group varied, and therefore considered it was hard to compare the two treatment arms. The Committee noted it was not possible to determine from the evidence which of the treatments within the physician's choice group were inferior to eribulin, and whether those treatments were relevant to the NZ treatment environment.

Many clinical trials test newer medicines against a range of chemotherapies selected as Treatment of Physician Choice (TPC). This is a standard methodology that is used worldwide, with results accepted as a valid demonstration of the properties of a medicine compared to standard of care that people normally receive. Recent examples are Destiny-Breast04 testing trastuzumab deruxtecan against TPC in the form of eribulin (51.1%), capecitabine (20.1%), gemcitabine (10.3%), nab-paclitaxel (10.3%) or paclitaxel (8.2%) and TROPICS-02 testing sacituzumab govitecan against TPC as eribulin (48%), vinorelbine (23%), capecitabine (8%) or gemcitabine (21%). The EMBRACE study demonstrated an overall survival benefit for eribulin over TPC. Prior therapies mostly included taxanes, anthracyclines and capecitabine, treatments very likely to have been administered to NZ patients needing further chemotherapy. The TPC comparators used in EMBRACE are representative of the current options available in New Zealand for 2nd line and beyond, and included vinorelbine (25%), gemcitabine (19%), capecitabine (18%), taxanes (15%), anthracyclines (10%), other chemotherapies (10%) and hormonal therapy (4%).

1.18 The Committee considered that the trials to support health benefit were heterogeneous in the number of prior treatment lines, which confounded the assessment of the effect of eribulin and impeded those trials' relevance to the New Zealand population and clinical setting. The Committee considered there was also heterogeneity in the control arm of the trials, which impacted on assessing benefit. The Committee considered that if the trials were undertaken now, the design would likely be different with results more likely to detect any health benefit where it might exist. The Committee considered that overall, it was difficult to draw conclusions from the available evidence and there was uncertainty about the quality of health benefit and whether this would result in health outcomes that were clinically meaningful.

As stated above it is unrealistic to expect that historical trials will have been designed to perfectly reflect a snapshot of the treatment history of NZ patients with advanced breast cancer, who will have received a variety of medicines in different sequences. The efficacy and safety of eribulin was demonstrated in pivotal trials, Study 305 (EMBRACE) and Study 301, both Phase 3 trials published in 2011 and 2013 respectively. One can speculate that trial design might be different today, but the data generated from this and other subsequent trials has led to registration of eribulin in over 70 countries including by Medsafe, TGA in Australia, EMA, FDA and Japan and its inclusion in international guidelines including ESMO, ASCO, NCCN and ABC NZ2. Further to this, there have been numerous RWE studies published since the pivotal clinical trials which have supported the results and shown efficacy and safety in various patient populations. As a result, eribulin is used as a standard of care chemotherapy by oncologists across the globe as made evident by these RWE studies and inclusion of eribulin in TPC comparator arms of new treatment clinical trials.

Patients with advanced breast cancer receive a variety of treatments deemed by their oncologists to be the most suitable for the individual, taking into account current health status, previous treatment history, tolerance of particular therapies, treatment response, likely side effects, disease burden, tumour location and suitability for a variety of reasons. Having supported many women with this disease, including BCAC Committee members and close friends, we have learned that oncologists need a variety of treatment options at different stages of advanced breast cancer to meet the individual needs for their diverse patients.

Through our experience we have a very clear understanding of the deep trauma experienced when patients are informed by their oncologist that they have run out of effective treatment options. We are asking here that another chemotherapy treatment option be added for these patients as lack of funded medicines creates a real and significant unmet health need. This treatment is currently available only to patients who can afford to pay for it in a private clinic. Those who cannot pay do not have access.

Suitability

1.19 The Committee noted that eribulin is administered as an intravenous infusion and therefore individuals will need to travel to infusion services for treatment.

The majority of medicines available for advanced breast cancer require infusion. Eribulin infusion is a rapid process taking only 2 – 5 minutes with no need for premedication. Eribulin can also be diluted and injected. Eribulin is a candidate for home administration as demonstrated in Australia (Peter MacCallum Centre) and the UK (The Christie NHS Foundation Trust). It may therefore also be suitable for administration in medical clinics closer to home as such services develop within the community.

Cost and savings

1.20. The Committee noted that should eribulin be funded it would be an additional treatment option, rather than replacing an existing one.

Yes, eribulin will be a much-needed chemotherapy option for patients likely nearing the end of their treatment journey.

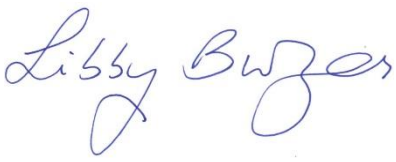
We note that eribulin has been in use internationally for more than 10 years and was funded in Australia in 2013. As an "older" medicine it is relatively inexpensive, compared with newer cancer medicines that have been more recently developed. Eisai, the pharmaceutical company that markets eribulin (Halaven) in New Zealand has established a low-cost patient access programme for this medicine, suggesting it would be available to Pharmac at a very reasonable price.

We ask that Pharmac approach Eisai representatives to discuss this.

1.21. The Committee considered that the number of individuals treated would be less than 300 a year.

We estimate that uptake would be considerably less than 300 per year and that treatment would generally continue for months, not years.

Ngā mihi,



Libby Burgess

BCAC Chair