Ombudsman
Fairness for all

Case note

Decisions of PHARMAC to fund Opdivo and Keytruda

Legislation	Ombudsmen Act 1975, New Zealand Public Health and Safety Act 2000
Agency	Pharmaceutical Management Agency (PHARMAC)
Ombudsman	Leo Donnelly
Case number(s)	428401
Date	December 2017

Summary

A complaint was made to the Ombudsman that PHARMAC took too long to approve the May 2015 application to fund the metastatic melanoma cancer drug Keytruda.[1] The complainant considered that PHARMAC gave insufficient consideration to the grave health needs of metastatic melanoma cancer patients, and delayed funding Keytruda in order to obtain a more competitive price. She considered that PHARMAC should have acknowledged the clinical efficacy of Keytruda at an earlier juncture and afforded it a higher priority rating, which may have improved health outcomes for metastatic melanoma cancer patients.

The complainant also considered that PHARMAC had not released credible information to explain the decision to fund another PD-1 inhibitor Opdivo[2] (from July 2016), and then to fund Keytruda (from September 2016). She stated that melanoma patients had not been aware of the Opdivo funding application and were '*very surprised*' when PHARMAC announced the decision to commence public consultation, on the same day as the government announced $50 million additional funding for PHARMAC. She considered that PHARMAC then also undertook a complete '*U-turn*' when it consulted on the funding of Keytruda in June 2016. She considered that families which lost loved ones in the period before any PD-1 inhibitor medicines were approved for funding by PHARMAC had no way of knowing if the decision-making process was fair.

[1] Keytruda is a PD-1 inhibitor, which is a relatively new class of drugs which activates the patient's immune system to attack cancer cells. The generic name for Keytruda is pembrolizumab.

[2] The generic name for Opdivo is nivolumab.

In September/November 2015, PHARMAC had received recommendations from relevant committees that the Keytruda application be funded as a low priority due to concerns about efficacy and cost. It was then ranked by PHARMAC in December 2015, and discussions with the supplier continued.[3] In early 2016, PHARMAC received a proposal for Opdivo which had better clinical evidence and more favourable commercial terms. From around February 2016, the clinical advice PHARMAC received suggested that PD-1 inhibitors had a similar therapeutic effect. PHARMAC subsequently reached agreements to fund Opdivo and Keytruda, with revised commercial terms. After separate processes of public consultation,[4] both medicines were approved for funding and listed on the pharmaceutical schedule.

The Ombudsman concluded that the manner in which PHARMAC prioritised the Keytruda application was not unreasonable, and was in accordance with its statutory objectives of obtaining the best health outcomes within the available funding. PHARMAC was entitled to rely on the expert advice it received from its clinical advisors, and used its position to negotiate prices with the two suppliers. It also took reasonable steps to keep the public informed of the progress of the two applications.

Background

1. PHARMAC's function is to '*secure for eligible people in need of pharmaceuticals the best health outcomes that are reasonably achievable from pharmaceutical treatment, within the amount of funding provided*.'[5] To do this, PHARMAC uses a decision-making framework known as the Factors for Consideration[6] to undertake a comparative analysis of all funding applications, which results in a confidential priority ranking. The Minister of Health is not able to direct PHARMAC to fund any specific medicines at any particular price.

2. Clinical advice is a key input into PHARMAC's decision-making processes. The principal source of clinical advice is the Pharmacology and Therapeutics Advisory Committee (PTAC) and its subcommittees. The Cancer Treatments Subcommittee of PTAC is known as "CaTSoP". These committees provide advice and recommendations to PHARMAC which are considered alongside all other relevant information. PHARMAC does not simply adopt the recommendations that it receives.

3. Medicines listed by PHARMAC in the pharmaceutical schedule are funded from the Combined Pharmaceutical Budget (CPB), which is set annually by the Minister of Health following consideration of the joint budget bid submitted by PHARMAC and district

[3] The PHARMAC priority list is confidential. It is reviewed on a quarterly basis, although it can be reviewed out of cycle if new evidence emerges. The cumulative total cost of the items on the priority list (in rank order) is then matched against available headroom in the Combined Pharmaceutical Budget to determine which investments PHARMAC will work on to progress for funding.

[4] Under PHARMAC operating policies, public consultation generally occurs after the medicine has been assessed, prioritised and a provisional deal is reached with the suppliers.

[5] Section 47(a) New Zealand Public Health and Disability Act 2000.

[6] https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/

health boards. PHARMAC's fixed budget precludes the funding of all potentially beneficial medicines that become available.

4. In May 2015, PHARMAC received an application from Merck Sharpe and Dohme (MSD) for the funding of Keytruda.

5. In September 2015, Medsafe registration was granted for Keytruda. Also in September 2015, CaTSoP recommended that the Keytruda application be funded with a low priority due to uncertainty about the longer-term benefits and the very high cost. In November 2015, PTAC also recommended funding Keytruda with low priority.

6. In December 2015, PHARMAC received advice from the Minister of Health of a likely additional $11 million in baseline funding for the 2016/2017 financial year. Also in December 2015, PHARMAC ranked Keytruda and published the clinical advice it had received from its committees on its website, stating that more reliable evidence of the benefits was required in order to justify an investment in Keytruda.

7. In February 2016, PHARMAC received an application from Bristol-Myers Squibb (BMS) for the funding of Opdivo. PTAC advised PHARMAC that Opdivo and Keytruda may have a similar therapeutic effect and recommended that advice be sought from CaTSoP. Later in the month, PHARMAC wrote to both suppliers (BMS and MSD) putting forward commercial proposals in equivalent terms.

8. In March 2016, PHARMAC notified the receipt of the Opdivo funding application on the *Application Tracker* page of its website but did not otherwise make any public announcement. Also in March 2016, a petition with 11,000 signatures was presented to Parliament, requesting that extra funding be granted to PHARMAC so that Keytruda could be made available. On 30 March 2016, in response to correspondence from MelNet[7]urging the funding of a PD-1 Inhibitor, PHARMAC confirmed that it was assessing a funding application for Opdivo and it was continuing to work with both suppliers.

9. PHARMAC reached provisional agreements (conditional on Board approval) with MSD and BMS for the funding of Keytruda and Opdivo on 20 April 2016. Two days later, CaTSoP recommended that Opdivo be funded for advanced melanoma with a medium/high priority. The clinical data was considered to be more reliable than that for Keytruda. It was noted that the two treatments would provide '*the same or similar*' therapeutic effect.

10. On 29 April 2016, the PHARMAC Board decided that PHARMAC should commence public consultation on the Opdivo provisional agreement and reopen negotiations on Keytruda.[8]

11. On 4 May 2016, the government announced an extra $50 million funding for PHARMAC. An $11 million increase in baseline funding was the result of the joint PHARMAC/DHBs

[7] The Melanoma Network of New Zealand.

[8] Medsafe registration for Opdivo was granted on 28 April 2016.

budget bid, and an additional $39 million came from participation in Treasury's Social Investment process.[9]

12. The same day, PHARMAC commenced public consultation on a proposal to fund Opdivo for patients with unresectable and metastatic melanoma from 1 July 2016. PHARMAC released supporting information stating that Opdivo was preferred to Keytruda because the clinical data was more reliable. On 5 and 6 May 2016, PTAC recommended that the Opdivo application be approved with medium priority, based on the strength and quality of evidence.

13. On 8 June 2016, the PHARMAC Board approved the funding of Opdivo, for listing on the pharmaceutical schedule from 1 July 2016. This was announced on 10 June 2016.

14. On 22 June 2016, PHARMAC reached a new provisional agreement with MSD (the supplier of Keytruda) on commercially favourable terms.

15. On 28 June 2016, PHARMAC commenced public consultation on a proposal to fund Keytruda from 1 September 2016. On 2 August 2016, PHARMAC announced the decision to fund Keytruda.

Investigation

16. PHARMAC was advised of Ombudsman Leo Donnelly's intention to investigate whether its consideration of funding applications for the treatment of metastatic melanoma was administratively sound. In response, it provided the Ombudsman with detailed information about its processes and the prioritisation of Keytruda and Opdivo. The Ombudsman carefully considered PHARMAC's comments in light of the issues raised by the complainant, which included:

    - Whether PHARMAC had focused on commercial imperatives at the expense of health outcomes for melanoma patients; and
    - Whether the process was sufficiently transparent.

17. The Ombudsman considered PHARMAC's comments that it did not regard Keytruda to be ineffective, but that the clinical evidence was not strong in terms of improvement to length of life. There were '*plenty of claims*' but PHARMAC needed to be confident about the enduring benefits. PHARMAC also knew that other new treatments would be coming onto the market. The clinical trial results for the Opdivo application were much stronger in terms of survival gain and the commercial terms were better, and this prompted PHARMAC to progress the Opdivo application and review its approach to Keytruda.

[9] In the particular context of the 2015/2016 budget round, PHARMAC was presented with a larger volume of '*good value for money*' funding options than in previous years. The Ministry of Health co-ordinated a bid on behalf of PHARMAC and the DHBs for additional funding via the Treasury's social investment process which resulted in the additional $39 million funding.

Throughout the process, PHARMAC staff actively encouraged competition between the two suppliers to get the best deal.

18. PHARMAC further explained that there was no express revision of PTAC's advice regarding Keytruda. Rather, CaTSoP and PTAC considered that the evidence base for Opdivo was superior to that for Keytruda as a result of the different studies that had been done. When combined with the conclusion that current evidence was consistent with the two products having '*same or similar efficacy*', this had an impact on the evaluation of Keytruda. This was reinforced by a consensus statement (received during the public consultation round on Opdivo) from 13 medical oncologists who considered that it was safe and clinically acceptable for patients to switch between the two treatments.

19. The Ombudsman also considered PHARMAC's explanation that it does not generally proactively release commercial information due to the commercial sensitivities which are usually involved. However, PHARMAC did acknowledge the value of public engagement and the importance of the public knowing what is going on, at least in general terms, and noted its proactive release of information about the progress of funding applications on its website. PHARMAC considers that there are '*numerous opportunities*' for interested parties to communicate and have input outside of public consultation processes. It has an established practice of releasing the clinical advice received from clinical advisory committees on specific proposals on its website, and often hears from treating clinicians, patient groups, and other stakeholders, prior to formal consultation on a proposal.

20. In this specific case, the Ombudsman noted PHARMAC's view that there was a '*very high level*' of public engagement with stakeholder groups (such as MelNet and the Cancer Society) concerning the Keytruda application and PD-1 Inhibitors in general. It had '*numerous meetings*' with cancer groups and clinicians and responded to a large volume of correspondence and media enquiries. The expert advice concerning Keytruda was published in order to inform debate and to convey PHARMAC's view that the benefits had been overstated.

Ombudsman's opinion

The prioritisation of Keytruda

21. The Ombudsman formed the opinion that PHARMAC did not allow commercial considerations to override the needs of cancer patients in its approach to prioritising Keytruda. PHARMAC was entitled to rely on the advice it received from its expert committees about the efficacy of Keytruda. There was no clear basis to suggest that the Keytruda application should have been accorded higher priority.

22. PHARMAC's evaluation of Keytruda shifted in early 2016 as a result of evidence about PD-1 inhibitors contained in the Opdivo application, rather than specific clinical trials demonstrating Keytruda's effectiveness. By this time, PHARMAC had also received an indication from the Minister of Health that it would likely receive additional funding

following its budget bid. PHARMAC then took all reasonable steps to ensure that a PD-1 inhibitor would be made available in New Zealand as soon as possible. In early 2016, PHARMAC asked its clinical advisor committees to consider whether Keytruda and Opdivo could be substituted for each other. The Opdivo proposal was advanced expeditiously, with public consultation commencing shortly after a provisional agreement was reached with BMS, as soon as additional funding for PHARMAC had been confirmed, and before the PTAC recommendation was received by PHARMAC.

23. PHARMAC was, more or less, in continual negotiations with MSD from February 2016 in order to find a commercially acceptable basis for funding Keytruda. PHARMAC staff reached a provisional agreement in April 2016 which was not ratified by the Board. PHARMAC eventually obtained more favourable commercial terms for Keytruda which resulted in a new provisional agreement in June 2016. The public consultation period for Keytruda commenced four days later. The funding of Keytruda was approved by the PHARMAC Board in July 2016.

The level of transparency

24. The Ombudsman formed the opinion that PHARMAC provided an adequate level of transparency and engagement. PHARMAC took a relatively open and transparent approach to processing the Keytruda application through 2015. In December 2015, PHARMAC released summary information on its website which stated that Keytruda was regarded as very expensive and there was a gap between the public's perception of the benefits offered by Keytruda and the measured benefits seen in the clinical trials to date. As a result, there was a high level of public awareness and debate about Keytruda with intensive lobbying about melanoma medicines, culminating in the petition to parliament.

25. In early 2016, PHARMAC took a more reactive approach to releasing information, due to the need to preserve the confidentiality of negotiations with suppliers, and because confirming that an additional funding package had been requested would have been unhelpful to the negotiations. The Opdivo application was not subject to the same level of public scrutiny as the Keytruda funding proposal. This meant that many melanoma patients and their families may have been unaware that PHARMAC had another option open to them. In this context, there were high levels of uncertainty and anxiety about whether PD-1 inhibitors would be funded in New Zealand.

26. However, PHARMAC did not treat the Opdivo application or the fact of negotiations with the suppliers as confidential. PHARMAC was open about the fact it had received the Opdivo proposal, although many cancer patients were not aware of it. The Opdivo application was notified on its website via Application Tracker on 1 March 2016. It was acknowledged in various other enquires and correspondence. The approach taken to the Keytruda application was not markedly dissimilar, with the exception that expert advice was released in late December 2015 and that the attention of lobbyists and media was fully engaged. The information released by PHARMAC enabled the public to participate in debate about melanoma treatments.

27. The Ombudsman noted that it was vitally important that the New Zealand public are provided with adequate information and that commercial considerations do not override transparency. Although PHARMAC's negotiating position would be prejudiced if detailed commercial information was released, and PHARMAC's processes are often complicated, it should be as open as possible about the progress of funding applications, particularly in cases of high public interest. PHARMAC has an important role that impacts on health options for the New Zealand public. It must keep New Zealanders adequately informed to promote transparency, accountability and public confidence in decision-making.

Outcome

28. The Ombudsman formed the final opinion that PHARMAC had not acted unreasonably. Keytruda and Opdivo were prioritised in a manner which was consistent with PHARMAC's statutory objectives of obtaining the best health outcomes within the available funding. Although the Keytruda application was given a higher profile, there was an adequate level of transparency concerning the Opdivo application which was notified on PHARMAC's website in early 2016. However, the Ombudsman asked PHARMAC to reflect on whether it could have been more open about the processing of the PD-1 Inhibitor funding applications, given that some patients with metastatic melanoma cancer were uncertain about how their interests were factored into the decision-making process.