WONDER DRUG CONSULTING

Analysis of PBAC submissions and outcomes for medicines for patients with cancer (2010-2016)

Report prepared for Medicines Australia Oncology Industry Taskforce

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EXECUTIVE SUMMARY

Timely access to new cancer medicines via the Pharmaceutical Benefits Scheme (PBS) remains an important public health care issue.

The objective of the project was to update the 2014 analysis of the local innovative pharmaceutical industry's submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) for new medicines for patients with cancer.

The methods for the project were, in most respects, the same as those described in the 2014 report. A number of new metrics were developed to provide deeper insights and thus progress thus the discussion on timely access.

The study period for the analysis was 2010 – 2016; where the initial major submission for a given medicine/patient population pairing was considered by the PBAC at or after the 2010/1 meeting. The study sample included all relevant submissions from the March 2016 meeting and all resubmissions from the July 2016 and August 2016 meetings; relevant initial submissions from the July 2016 and August 2016 meetings were not considered.

The analysis included PBS listings up to and including 1 October 2016.

Insofar as cancer medicines can be used to treat patients with different cancers or even different stages of the same cancer, the analysis was based on medicine/patient population pairings.

The PBAC considered 147 'high-level' cancer submissions during the study period. There were more initial submissions than there were resubmissions. There were more submissions for new medicines than there were submissions for new indications.

The 147 'high-level' submissions yielded 177 PBAC outcomes. The annual recommendation rate varied from year to year but was never greater than 50%. The recommendation rate was greater than the rejection rate in 2012 & 2013; in all other years it was less. Overall, the recommendation rate was below the rejection rate. The overall deferral rate was two thirds of the recommendation rate.

A few recommended medicine/patient population pairings were associated with one or more 'conditions' that resulted in a resubmission from the sponsor concerned.

49 of the 64 recommendations had resulted in a listing in the Schedule of Pharmaceutical Benefits as at 1 October 2016.

Of the 64 recommendations, 57 were recommended as requested and 7 were recommended on a different basis.

Of the 113 rejections and deferrals, the most common initial reasons were uncertain clinical benefit (rejection), uncertain cost effectiveness (rejection) and further analysis/consultation required (deferral).

The results indicate that on average, a new cancer medicine is listed on the PBS about two years after the initial PBAC submission. The evidence does not indicate a different period for a new cancer medicine when compared with the corresponding period for a new cancer indication.

On average, a new cancer medicine is listed on the PBS about two years after its registration by the TGA. The evidence indicates a seven-month shorter period for a new cancer medicine than the corresponding period for a new cancer indication.

The average period from the date of PBAC recommendation to date of PBS listing for a new cancer medicine/indication was over seven months.

Eight recommended medicine/patient population pairings are yet to be listed; four are from the March 2016 PBAC meeting. The average period is over a year due to outstanding recommendations from 2013 and 2015.

An analysis of the recommended medicine/patient population pairings that resulted in a PBS listing revealed that, on average, it spent more time in the realm of Government (37%) and with the PBAC (35%) than it did the relevant sponsor (27%).

INTRODUCTION

The Oncology Industry Taskforce (OIT) of Medicines Australia has commissioned Wonder Drug Consulting Pty Ltd (WDC) to prepare a report on access to new cancer medicines in Australia. WDC conducted an analysis on this issue in 2014.

Timely access to new cancer medicines via the Pharmaceutical Benefits Scheme (PBS) remains an important public health care issue.

The objective of the project was to update the 2014 analysis of the local innovative pharmaceutical industry's submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) for new medicines for patients with cancer.

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METHODS

The methods for the project were, in most respects, the same as those described in the 2014 report.

The study sample or the analysis was the collection of submissions to the PBAC for medicines for patients with cancer in a given period. Submissions for medicines that are also used predominantly or even exclusively by patients with cancer (e.g. anti-nauseants, colony-stimulating factors, anti-resorptive agents and antidotes) were excluded.

The definition of cancer included solid tumours and 'liquid' tumours or blood cancers (e.g. leukaemias & lymphomas).

While myelofibrosis and myelodysplastic syndrome were considered to be 'cancers' and submissions for these diseases were included, paroxysmal nocturnal haemoglobinuria (PHN) and atypical haemolytic uraemia syndrome (aHuS) were not and thus submissions for these diseases were excluded.

The focus of the analysis was submissions for new medicines (i.e. new listings) and new indications (i.e. new use within a given cancer (e.g. extend use from second-line to first-line) and across cancers (extend use from breast cancer to include lung cancer). While most of the submissions in this category were major submissions; some were minor submissions (i.e. minor resubmissions). As per the 2014 report, these initial major and subsequent major or minor submissions will be referred to in this report as 'high-level' submissions.

Submissions that were withdrawn by a sponsor before a PBAC meeting were excluded; the study sample was therefore comprised of submissions that were actually considered by the PBAC.

The 2014 submissions for trastuzumab (Herceptin) seeking to transfer subsidy from Medicare to the PBS were excluded. Trastuzumab emtansine (Kadcyla) was considered to be a new medicine so submissions relating to its listing on the PBS were included.

Submissions relating to a pricing and/or a managed entry scheme issue for a listed cancer medicine were excluded.

Insofar as cancer medicines can be used to treat patients with different cancers or even different stages of the same cancer, the analysis was based on medicine/patient population pairings.

The study period for the analysis was 2010 – 2016; where the initial major submission for a given medicine/patient population pairing was considered by the PBAC at or after the 2010/1 meeting. The study sample included all relevant submissions from the March 2016 meeting and all resubmissions from the July 2016 and August 2016 meetings; relevant initial submissions from the July 2016 and August 2016 meetings were not considered.

This study period eliminated many of the outlying contentious submission sequences, such as:

- Cetuximab (Erbitux) for metastatic colorectal cancer
- Everolimus (Afinitor) for renal cell carcinoma
- Panitumumab (Vectibix) for metastatic colorectal cancer
- Sorafenib tosylate (Nexavar) for renal cell carcinoma

The initial submissions for these medicine/patient population pairings were considered by the PBAC before 2010. The inclusion of these medicine/patient population pairings in the 2014 analysis was somewhat contentious insofar as they were all associated with multiple resubmissions, often with extended periods between resubmissions. The initial submission for cetuximab was considered by the PBAC in early 2005; it could be argued that the inclusion of the multiple submissions for cetuximab in the study sample may not be reflective of current PBAC decision-making. The exclusion of these submissions from the analysis is conservative insofar as their inclusion would have extended the time period from date of initial submission or date of registration to date of PBS listing.

The analysis included PBS listings up to and including 1 October 2016.

The TGA and PBS websites and serial issues of the Schedule of Pharmaceutical Benefits were examined to collect the following data for each medicine/patient population pairing:

- Date of registration (TGA decision date/ARTG start date) – TGA website
- Date of submission/s (it will be assumed that the date of a given submission was the date of the advertised PBAC cut-off for major/minor submissions) – PBS calendar
- Outcome/s (recommendation, rejection, deferral) – PBAC outcomes
- Date of outcome/s – PBS calendar
- Main (initial) reason for outcome (rejection or deferral) – PBAC Public Summary Document
- Date of PBS listing – Schedule of Pharmaceutical Benefits

The analysis assessed the performance of submissions on a number of metrics:

- Number of submissions (overall, new cancer medicines, new cancer indications)
- Number of outcomes (overall, new cancer medicines, new cancer indications). Breakdown by outcome type (recommendation, rejection, deferral)
- Number of PBS listings (overall, new cancer medicines, new cancer indications)
- Main (initial) reason for outcome
- Time from the date of the initial submission to the date of PBS listing (overall, new cancer medicines, new cancer indications)
- Time from the date of the initial PBAC submission to the date of the last PBAC outcome (overall, new cancer medicines, new cancer indications).
- Time spent (proportion of overall time) with the sponsor, the PBAC and the Department/Cabinet (i.e. post PBAC) (only for submissions that resulted in a PBS listing)

- Time from the date of TGA registration to the date of PBS listing (overall, new cancer medicine, new cancer indications)
- Time from the date of PBAC recommendation to the date of PBS listing (overall, new cancer medicines, new cancer indications)
- Time from the date of PBAC recommendation to the current date (for those awaiting listing; overall, new cancer medicines, new cancer indications)

Submissions can include multiple requests and thus yield multiple outcomes so the number of outcomes and PBS listings can at times be greater than the number of submissions. Submissions with multiple requests may differ with respect to:

- Type of request (e.g. new indication, new formulation, restriction change, etc.)
- Request number (e.g. one request may be an initial request, the other/s may be repeat requests)
- Outcome (e.g. one request might be accepted by the PBAC (i.e. recommended), whereas the other/s might not (e.g. rejected)
- Implementation (e.g. all of the recommendations might not result in a PBS listing, or they might be listed at different times)

For submissions with two requests, for example, one request was for a new listing and the other was for a new indication, a portion (i.e. half) of the submission was allocated to each request. This means that for some metrics, the number of submissions might not be a whole number.

While it is possible to have non-whole numbers for submissions (e.g. a submission with two requests; one is an initial request for the listing of a medicine for a new patient population, the other for the same medicine but is a repeat request for another new patient population), it is not possible to have partial PBS listings.

RESULTS

Metric 1 – Number of submissions

The PBAC considered 147 'high-level' cancer submissions during the study period. There were slightly more initial submissions than there were resubmissions. There were more submissions for new medicines than there were submissions for new indications (Table 1).

Table 1 – 'High-level' PBAC submissions for medicines for patients with cancer that were considered by the PBAC (2010-2016)

Year	Number of PBAC meetings*	Number of submissions considered by the PBAC#	Number of initial submissions considered by the PBAC	Number of resubmissions considered by the PBAC	Number of submissions for new medicines (n)	Number of submissions for new indications (n)
2010	5	9	7	2	2	7
2011	5	15	12	3	6	9
2012	3	18	7.5	10.5	8	10
2013	5	26.5	11.5	15	12.5	14
2014	3	26.5	13	13.5	20	6.4
2015	3	32	19	13	20	12
2016**	2	20	6.5	13.5	14	6
2010-2016	**26**	**147**	**76.5 (52%)**	**70.5 (48%)**	**82.5 (56%)**	**64.5 (44%)**

* Scheduled and unscheduled (i.e. out of session and extra-ordinary) meetings

** **Initial** submissions from the July and August meetings were excluded

Metric 2 – PBAC outcomes for high-level submissions for medicines for patients with cancer

The 147 'high-level' submissions yielded 177 PBAC outcomes (Table 2). The number of outcomes for a given PBAC meeting/study period can exceed the number of submissions considered by the PBAC for the same meeting/study period as a result of:

- A submission resulting in a listing in different sections of the Schedule of Pharmaceutical Benefits with different restrictions (e.g. unrestricted listing in one section and a restricted benefit listing in another section)
- A submission having multiple requests for the same medicine (e.g. a request to list the medicine in two discrete patient populations); the PBAC might have accepted (i.e. recommended) one request but rejected the other
- A submission having multiple requests for multiple, related medicines that have the same sponsor

Table 2 outlines the PBAC outcomes for the 147 'high-level' submissions for medicines for patients with cancer. It shows that their success rate was low with the rejection rate being higher than the recommendation rate in three of the seven years between 2010 and 2016.

Table 2 – PBAC outcomes for the 147 'high-level' submissions for medicines for patients with cancer (2010-2016)

Period	PBAC outcome				
	Recommendation (%)	Rejection (%)	Deferral (%)	No outcome (%)	Total
2010	2 (22%)	5 (56%)	2 (22%)	0 (0%)	9
2011	3 (20%)	11 (73%)	1 (9%)	0 (0%)	15
2012	8 (42%)	7 (37%)	4 (21%)	0 (0%)	19
2013	14 (44%)	10 (31%)	8 (25%)	0 (0%)	32
2014	13 (40%)	8 (25%)	11 (35%)	0 (0%)	32
2015	14 (30%)	20 (43%)	11 (27%)	0 (0%)	45
2016	10 (40%)	9 (35%)	6 (25%)	0 (0%)	25
2010-2016	**64 (36%)**	**70 (40%)**	**43 (24%)**	**0 (0%)**	**177**

The annual recommendation rate varied from year to year but was never greater than 50%. The recommendation rate was lower than the rejection rate in 2010, 2011 and 2015. Overall, the recommendation rate was slightly below the rejection rate. The overall deferral rate was two thirds of the recommendation rate.

Table 3 outlines the PBAC outcomes for the 82.5 'high-level' submissions for new medicines for patients with cancer.

Table 3 – PBAC outcomes for the 82.5 'high-level' submissions for new medicines for patients with cancer

Period	PBAC outcome				
	Recommendation (%)	Rejection (%)	Deferral (%)	No outcome (%)	Total
2010	1 (50%)	1 (50%)	0 (0%)	0 (0%)	2
2011	0 (0%)	6 (100%)	0 (0%)	0 (0%)	6
2012	6 (75%)	1 (12%)	1 (12%)	0 (0%)	8
2013	3 (20%)	8 (53%)	4 (27%)	0 (0%)	15
2014	10 (40%)	4 (16%)	11 (44%)	0 (0%)	25
2015	11 (35%)	13 (42%)	7 (23%)	0 (0%)	31
2016	7 (37%)	6 (32%)	6 (32%)	0 (0%)	19
2010-2016	**38 (36%)**	**39 (36%)**	**30 (28%)**	**0 (0%)**	**107**

The annual recommendation rate varied from year to year. The recommendation rate was greater than the rejection rate in 2012, 2014 and 2016; in the other years it was less. Overall, the recommendation rate and the rejection rates were comparable. The overall deferral rate was below the recommendation rate.

Table 4 outlines the PBAC outcomes for the 64.5 high level submissions for new indications for patients with cancer.

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Table 4 – PBAC outcomes for the 64.5 'high-level' submissions for new indications for patients with cancer

Period	PBAC outcome				
	Recommendation (%)	Rejection (%)	Deferral (%)	No outcome (%)	Total
2010	1 (14%)	4 (57%)	2 (29%)	0 (0%)	7
2011	3 (33%)	5 (56%)	1 (11%)	0 (0%)	9
2012	2 (17%)	6 (56%)	3 (27%)	0 (0%)	11
2013	11 (65%)	2 (12%)	4 (23%)	0 (0%)	17
2014	3 (43%)	4 (57%)	0 (0%)	0 (0%)	7
2015	3 (23%)	7 (54%)	3 (23%)	0 (0%)	13
2016	3 (50%)	3 (50%)	0	0 (0%)	6
2010-2016	**26 (37%)**	**31 (44%)**	**13 (19%)**	**0 (0%)**	**70**

The annual recommendation rate varied from year to year. The recommendation rate was greater than the rejection rate in 2013; in all other years it was less, apart from 2016 where it was comparable. Overall, the recommendation rate was below the rejection rate. The overall deferral rate was about half the recommendation rate.

A few recommended medicine/patient population pairings were associated with one or more 'conditions' that resulted in a resubmission from the sponsor concerned (Table 5).

Table 5 – PBAC recommended medicine/patient population pairings with an associated resubmission

Medicine	Cancer	Initial PBAC meeting (recommendation)	Subsequent PBAC meeting/s	Subsequent PBAC outcome/s
Abiraterone acetate	Prostate	2012/1	2012/2, 2012/3	Recommendation, Recommendation
Afatinib dimaleate	Non-small-cell lung (first-line or later-line)	2013/E2	2015/1	Rejection*
Bevacizumab	Ovarian	2013/3	2014/1	Rejection
Brentuximab vedotin	Non-Hodgkin's lymphoma	2014/1	2014/2	Recommendation
Bendamustine hydrochloride	Non-Hodgkin's lymphoma (mantle cell)	2015/2	2015/3	No outcome (submission was withdrawn)
Bendamustine hydrochloride	Non-Hodgkin's lymphoma (indolent)	2015/2	2015/3	No outcome (submission was withdrawn)

* Resubmission requested a listing for patients with a discrete mutation

Metric 3 - Number of PBS listings

49 of the 64 recommendations (77%) for new medicines and new indications had resulted in a listing in the Schedule of Pharmaceutical Benefits as at 1 October 2016 (Table 6).

Table 6 – PBS listings

Year of PBAC recommendation	Number of PBS listings*
2010	2
2011	3
2012	6
2013	13
2014	12
2015	11
2016	2
2010 - 2016	**49**

* Two medicines (abiraterone acetate and brentuximab vedotin) were recommended multiple times for the same patient population; the last recommendation was deemed to have resulted in a PBS listing.

Metric 4 – Initial reason for outcome

The public summary document for each medicine/patient population pairing was examined to determine the **initial** reason for the PBAC outcome. Insofar as submissions are often rejected for **multiple** reasons, the initial reason might not have been the **only** reason or the **main** reason; it is simply the reason first mentioned.

The following hierarchal decision-making framework was used to determine the **initial** reason for a rejection or deferral (Table 7).

Table 7 – PBAC hierarchical decision-making framework (rejection or deferral)

Criterion category	Criterion
Clinical need	No clinical need, uncertain clinical need
Target patient population	Uncertain target patient population, incorrect target patient population, target patient population inadequately specified
Comparison	Incorrect proposed main comparator, additional comparison/s required, incorrect weighting of comparators
Clinical benefit	Uncertain clinical benefit, different clinical benefit
Economic benefit	No economic evaluation, incorrect economic evaluation method, uncertain cost effectiveness, unacceptable cost effectiveness
Budget impact	Uncertain budget impact, likely under-estimate, likely over-estimate
Other	Quality use of medicines issue, further analysis/consultation required

Each recommended medicine/patient population pairing was also examined to determine the nature of the outcome:

- Recommended as requested (i.e. the clinical and economic claims made by the sponsor in the submission were accepted). This does not necessarily mean the medicine was recommended at the requested price.
- Recommended on a different basis (i.e. the clinical and/or economic claim made by the sponsor in the submission was/were not accepted)

Whilst the framework provides some valuable insights into the Committee's decisions, it is important to note that it does not provide a full account of a given decision, especially for instances where a medicine was rejected for multiple reasons. At the present time, it is not possible for observers/stakeholders to be able to draw conclusions as to the most important reason/s for a specific medicine from the information that is currently in the public domain.

Summary statistics for the initial reason for the PBAC outcome for each medicine/patient population pairing are provided in Table 8.

Table 8 – Initial reason for PBAC outcome

Year	2010	2011	2012	2013	2014	2015	2016	2010-2016
Recommended as requested	2	2	5	12	12	14	7	57 (33%)
Recommended on a different basis	0	1	3	2	1	0	0	7 (4%)
Uncertain clinical need	0	0	0	0	0	0	0	0 (0%)
Uncertain target patient population	0	2	1	5	4	3	0	15 (8%)
Target patient population insufficiently described/defined	1	0	0	0	4	1	1	7 (4%)
Incorrect proposed main comparator	0	3	1	1	0	3	0	8 (5%)
Additional comparison/s required	0	0	0	0	1	0	0	1 (1%)
Uncertain clinical benefit	3	0	2	3	3	13	3	27 (15%)
Uncertain cost effectiveness	1	6	4	0	3	4	2	21 (12%)
Unacceptable cost effectiveness	0	0	0	3	1	1	2	7 (4%)
Further analysis/consultation required	2	1	3	6	3	5	5	27 (15%)

This metric examines all outcomes (i.e. recommendations) rather than the number of medicine/patient populations that obtained a recommendation.

Of the 64 recommendations, 57 were recommended as requested and seven were recommended on a different basis.

Of the 113 rejections and deferrals, the most common initial reasons were uncertain clinical benefit (rejection), uncertain cost effectiveness (rejection) and further analysis/consultation required (deferral).

Metrics 5 – 9 – Time to event analyses

The key milestone events for time to event analyses are:

- Date of TGA registration (Date of registration considered to be the 'date of decision'; dates obtained from the medicine's Australian Public Assessment Report)
- Date of initial PBAC submission (Date of PBAC submissions are not readily available; date of submission considered to be date of PBAC cut-off. Cut-off dates obtained from PBS calendar on PBS website)
- Date of PBAC recommendation (Date of PBAC recommendation not known with exact precision given scheduled PBAC meetings last 3 days; date of PBAC recommendation considered to be last day of scheduled meeting. PBAC meeting dates obtained from PBS calendar on PBS website)
- Date of PBS listing. PBS listing dates obtained from serial issues of the Schedule of Pharmaceutical Benefits.

The results for the various time-to-event analyses are presented in Table 9 below.

Table 9 – Time to event analyses (2010-2016)

Time to event analysis	Metric number	Overall	New cancer medicine	New cancer indication
Period from date of initial PBAC submission to date of PBS listing (months)*	5	20.5 (49)	20.9 (24)	20.1 (25)
Period from date of initial PBAC submission to date of last PBAC outcome (months)*	6	11.6 (90)	12.3 (47)	10.9 (43)
Period from date of TGA registration to date of PBS listing (months)	7	22.2 (49)	18.6 (24)	25.7 (25)
Period from date of PBAC recommendation to date of PBS listing (months)	8	7.4 (49)	7.6 (24)	7.3 (25)
Period from date of PBAC recommendation to current date (months)	9	13.7 (8)	14.6 (7)	6.7 (1)

Metric 5 – Period from the date of initial PBAC submission to the date of PBS listing

This metric does not consider high-level submissions that have been recommended by the PBAC but are yet to be listed. Likewise it does not include applications that remain deferred or rejected.

The results indicate that on average, a new cancer medicine is listed on the PBS about two years after the initial PBAC submission. The evidence does not indicate a different period for a new cancer medicine (n =24; 20.9 months) when compared with the corresponding period for a new cancer indication (n = 25; 20.1 months).

Metric 6 – Period from the date of initial PBAC submission to date of the last PBAC outcome

This metric includes all submissions and their related outcomes. There are a small number of applications where there was one or more resubmissions following a recommendation; the date of the last PBAC outcome was used.

On average, the evaluation process period (i.e. the period from date of initial submission to date of the last PBAC outcome) for a new cancer medicine or a new cancer indication was 11.4 months.

Metric 7 – Period from the date of TGA registration to the date of PBS listing

This metric does not consider high-level submissions that have been recommended by the PBAC but are yet to be listed. Likewise it does not include applications that remain deferred or rejected.

The results indicate that on average, a new cancer medicine is listed on the PBS about two years after its registration by the TGA. The evidence indicates a seven-month shorter period for a new cancer medicine than for a new cancer indication.

The shorter values for the period from the date of initial submission to date of PBS listing when compared with the corresponding value for the period from date of TGA registration to date of PBS listing reflect the sponsors' limited use of the TGA-PBAC parallel processes.

Metric 8 – Period from the date of PBAC recommendation to the date of PBS listing

This metric does not consider high-level submissions that have been recommended by the PBAC but are yet to be listed. Likewise it does not include applications that remain deferred or rejected.

The average period from the date of PBAC recommendation to date of PBS listing for a new cancer medicine/indication was over seven months. In an ideal world, this would be around five months.

Metric 9 – Period from the date of PBAC recommendation to current date

The study sample is medicine/patient population pairings that have been recommended by PBAC but have not yet been listed on the PBS (as at 1 October 2016).

This metric does not include initial recommendations for abiraterone acetate and brentuximab vedotin; both were listed on the basis of a further recommendation.

Eight recommended medicine/patient population pairings are yet to be listed; four are from the March 2016 PBAC meeting. The average period is over a year due to outstanding recommendations from 2013 and 2015.

Time analysis

The analysis was conducted on the medicine/patient population pairings that resulted in a PBS listing. The analysis sought to determine time the application was lead by the:

- Sponsor – the time period between submissions. No time was allocated to the sponsor if the initial submission was accepted by the PBAC (i.e. recommended) and proceeded to a PBS listing
- PBAC – the time period between the date/s of submission/s and the date/s of outcome/s. With a few exceptions (see below), the last outcome needed to be a recommendation.
- Government – the time period from the date of the (last) PBAC recommendation to the date of PBS listing.

This division of responsibility is not perfect insofar as some of the responsibility for a submission post PBAC recommendation also lies with the sponsor. It is unclear whether some of the time spent in the post-PBAC process is due to a sponsor's

inability to accept the conditions of the PBAC or related to unspecified timelines at the Department of Health. Nonetheless, it is in the sponsor's best interest to proceed to a PBS listing without delay, so it is reasonable to assign greater responsibility to the Government.

Some minor assumptions with respect to submission and outcome dates were required for a small number of submissions that were considered by the PBAC at extra-ordinary/out-of-session meetings.

Some adjustments were also made for a few applications:

- Abiraterone acetate for the treatment of patients with prostate cancer– it was assumed that its PBS listing proceeded from the final (fourth) outcome. The time period spent with the Government commenced from the date of the final outcome.
- Bevacizumab for the treatment of patients with ovarian cancer – insofar as the resubmission was rejected, its PBS listing proceeded from the recommendation from the initial submission. The time period spent with Government commenced from the date of the initial outcome.
- Brentuximab vedotin for the treatment of patients with non–Hodgkin's lymphoma - insofar as the resubmission was rejected, its PBS listing proceeded from the recommendation from initial submission. The time period spent with Government commenced from the date of the initial outcome.
- Bendamustine hydrochloride for the treatment of patients with non-Hodgkin's lymphoma – the third submission was withdrawn and hence was not considered.

It could be argued that for bevacizumab and brentuximab vedotin, the time period spent with the Government should have commenced from the date of the second outcome or should have been shared between the sponsor and the Government. Given the overall sample size (n = 49), the number of unusual examples (n = 2) and the fact that the PBAC considered resubmissions for these medicines at the following meeting, the use of different dates for bevacizumab and brentuximab vedotin will not have a major bearing on the analysis. Additional analyses using different commencement dates for these two medicines have therefore not been performed.

The results for this metric are presented in Table 10.

Table 10 – Time analysis

Attribute	Sponsor	PBAC	Government
Time (days)	8,251	10,750	11,487
Proportion (%)	27	35	38

The results indicate that, on average, a recommended medicine/patient population pairing spent more time in the realm of Government or PBAC than it did the relevant sponsor.

DISCUSSION

The 2016 report provides insights into the success rates and related timelines for submissions for new cancer medicines and new cancer indications that have been considered by the PBAC since 2010. The study period was updated to reflect current trends and to eliminate outliers that would no doubt have an effect on mean values. Additional metrics have also been developed to provide further insights that will hopefully advance the current debate on timely access to new cancer medicines on the PBS.

The PBAC considered 147 'high-level' cancer submissions during the study period. The number of submissions of 'high-level' cancer submissions considered by the PBAC on an annual basis has clearly risen over time and is set to continue.

The recommendation rate of the 'high level' submissions was 36% for the whole study period and was slightly lower than the corresponding rate for rejections (40%). Whilst the annual success rate fluctuated somewhat (20-44%), it was never greater than 50%.

The annual recommendation rate for the 'high-level' submissions for new cancer medicines varied from year to year. Overall, the recommendation rate was comparable to the rejection rate. The overall deferral rate was just below the recommendation rate.

Likewise, the annual recommendation rate for the 'high-level' submissions for new cancer indications varied from year to year. Overall, the recommendation rate was below the rejection rate. Again, the overall deferral rate was about half the recommendation rate.

49 (77%) of the 64 recommendations had resulted in a listing in the Schedule of Pharmaceutical Benefits as at 1 October 2016.

A conceptual framework was developed to explore the reasons behind the PBAC's outcomes in further detail and thus advance the discussion. Whilst the framework provides some valuable insights into the Committee's decisions, it is important to note that it does not provide a full account of a given decision, especially for instances where a given medicine was rejected for multiple reasons. At the present time, it is not possible for observers/stakeholders to be able to draw conclusions as to the most important reason/s for a specific medicine from the information that is currently in the public domain.

57 (89%) of the recommended medicine/patient population pairings were recommended as requested by the applicant; seven (11%) were recommended on a different clinical and/or economic basis.

Of the 113 rejections and deferrals, the most common **initial** reasons were uncertain clinical benefit (rejection), uncertain cost effectiveness (rejection) and further analysis/consultation required (deferral). Many of the medicine/patient population pairings that were rejected on the basis of uncertain clinical benefit were also rejected on the basis of uncertain or unacceptable cost effectiveness. There is no evidence to indicate that more submissions are being rejected initially on the basis of uncertain or unacceptable cost-effectiveness.

The results from the time-to event analysis are presented as mean values; some

medicine/patient populations in a given study sample performed better than the mean, others worse. It is also important to note that the study sample varied with each analysis.

The results indicate that on average, a cancer medicine is listed on the PBS 21 months after the initial PBAC submission. The available evidence does not indicate a different period for a new cancer medicine (n =24; 20.9 months) when compared with the corresponding period for a new cancer indication (n = 25; 20.1 months).

On average, the evaluation process period (i.e. the period from the date of initial submission to the date of the last PBAC outcome) for a new a new cancer medicine or a new cancer indication was just under a year.

The results indicate that on average, a cancer medicine is listed on the PBS 22 months after its registration by the TGA. The finding that the average period from the date of initial PBAC submission to date of PBS listing is shorter than the average period from the date of TGA registration to the date of PBS listing indicates sponsor companies are not making full use of the TGA-PBAC parallel process. The results indicate an average shorter period for a new cancer medicine than the corresponding period for a new cancer indication. This finding is consistent with the previous analysis; the average period for a new medicine was 19.4 months and 24.5 months for a new indication.

The average period from the date of PBAC recommendation to the date of PBS listing for a new cancer medicine/indication was over seven months. In an ideal world, this would around five months.

Eight recommended medicine/patient population pairings are yet to be listed; on average they have been unresolved for almost a year. Most of these outstanding recommendations are from the March 2016 PBAC meeting.

An analysis of the recommended medicine/patient population pairings that resulted in a PBS listing revealed that, on average, it spent slightly more time in the realm of Government (37%) and the PBAC (35%) than with the relevant sponsor (27%).

APPENDIX

Appendix 1 – PBS listings

Medicine	Cancer	Number of submissions before initial recommendation	Final PBAC meeting	Date of PBS listing
Degarelix acetate (Firmagon)	Prostate cancer	1	March 2010	1/12/2010
Rituximab (MabThera)	Chronic lymphocytic leukaemia	3	December 2010	1/12/2011
Bortezomib (Velcade)	Multiple myeloma	2	July 2011	1/12/2012
Dasatinib monohydrate (Sprycel)	Chronic myeloid leukaemia	1	July 2011	1/04/2012
Nilotinib hydrochloride monohydrate (Tasigna)	Chronic myeloid leukaemia	1	July 2011	1/04/2012
Bortezomib (Velcade)	Multiple myeloma	1	March 2012	1/10/2012
Cabazitaxel (Jevtana)	Prostate cancer	3	March 2012	1/08/2012
Pazopanib hydrochloride (Votrient)	Renal cell carcinoma	2	March 2012	1/10/2012
Trastuzumab (Herceptin)	Neo-adjuvant therapy for breast cancer	1	July 2012	1/12/2012
Abiraterone acetate (Zytiga)	Prostate cancer	2	November 2012	1/08/2013
Ipilimumab (Yervoy)	Malignant melanoma	3	November 2012	1/08/2013
Lenalidomide (Revlimid)	Myelodysplastic syndrome	3	March 2013	1/10/2013
Vinorelbine tartrate (Navelbine)	Breast cancer (monotherapy & combination)	2	March 2013	1/08/2013
Everolimus (Afinitor)	Tuberous sclerosis complex	2	April 2013	1/12/2013
Dabrafenib mesylate (Tafinlar)	Malignant melanoma	2	July 2013	1/12/2013
Pazopanib hydrochloride (Votrient)	Sarcoma	2	July 2013	1/03/2014
Sunitinib maleate	Pancreatic neuroendocrine	4	August 2013	1/12/2013

(Sutent)	tumour			
Erlotinib hydrochloride (Tarceva)	Non-small-cell lung cancer	3	August 2013	1/01/2014
Gefitinib (Iressa)	Non-small-cell lung cancer (initiation & maintenance)	4	August 2013	1/01/2014
Everolimus (Afinitor)	Breast cancer	3	August 2013	1/06/2014
Bevacizumab (Avastin)	Ovarian cancer	1	November 2013	1/08/2014
Eribulin mesylate (Halaven)	Breast cancer	2	November 2013	1/10/2014
Panitumumab (Vectibix)	Colorectal cancer	3	November 2013	1/04/2014
Everolimus (Afinitor)	Pancreatic neuroendocrine tumour	2	March 2014	1/04/2015
Paclitaxel (nanoparticle albumin bound)	Pancreatic cancer	1	March 2014	1/11/2014
Brentuximab vedotin (Adcetris)	Non-Hodgkin's lymphoma	2	July 2014	1/12/2014
Enzalutamide (Xtandi)	Prostate cancer	1	July 2014	1/12/2014
Axitinib (Inlyta)	Renal cell carcinoma	2	November 2014	1/12/2015
Cetuximab (Erbitux)	Colorectal cancer	1	November 2014	1/06/2015
Crizotinib (Xalkori)	Non-small-cell lung cancer	3	November 2014	1/07/2015
Ofatumumab acetate (Arzerra)	Chronic lymphocytic leukaemia	1	November 2014	1/04/2015
Pertuzumab (Perjeta)	Breast cancer	2	November 2014	1/07/2015
Pomalidomide (Pomalyst)	Multiple myeloma	2	November 2014	1/08/2015
Trametinib dimethyl sulphoxide (Mekinist)	Malignant melanoma	2	November 2014	1/08/2015
Trastuzumab emtansine (Kadcyla)	Breast cancer	4	November 2014	1/07/2015
Obinutuzumab (Gazyva)	Chronic lymphocytic leukaemia	2	November 2014	1/08/2015
Panitumumab (Vectibix)	Colorectal cancer	3	November 2014	1/10/2015
Pembrolizumab (Keytruda)	Malignant melanoma	1	March 2015	1/09/2015

Ruxolitinib phosphate (Jakavi)	Myelofibrosis (primary myelofibrosis, post-polycythemia vera myelofibrosis, post-essential thrombocythemia myelofibrosis)	3	March 2015	1/02/2016
Bendamustine hydrochloride (Ribomustin)	Non-Hodgkin's lymphoma, Mantle cell lymphoma	2	July 2015	1/05/2015
Trastuzumab (Herceptin)	Gastric cancer	3	July 2015	1/01/2016
Arsenic trioxide (Phenasen)	Acute promyelocytic leukaemia	1	November 2015	1/04/2016
Nivolumab (Opdivo)	Malignant melanoma	2	November 2015	1/05/2016
Bevacizumab (Avastin)	Cervical cancer	2	March 2016	1/09/2016
Tamoxifen citrate (Novadex-D)	Breast cancer	1	March 2016	1/10/2016