WONDER DRUG CONSULTING

Analysis of submissions and outcomes for medicines for patients with cancer; an international comparison (2010-2016)

Report prepared for Medicines Australia Oncology Industry

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EXECUTIVE SUMMARY

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

The objective of the project was to update the 2014 analysis of submissions for new medicines for patients with cancer to the Pharmaceutical Benefits Advisory Committee (PBAC) and other comparable health technology assessment (HTA) committees/agencies.

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 HTA agencies selected for the comparison were:

- The Pan Canadian Oncology Drug Review (pCODR) Expert Review Committee (pCERC) in Canada
- The National Institute of Health and Care Excellence (NICE) in England
- The Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care; IQWiG) and the Gemeinsamer Bundesausschuss (G-BA) in Germany
- The Transparency Commission (TC) in France

The analysis captures outcomes made by these agencies for the medicine/patient population pairings in the study sample up and including 1 October 2016. Final HTA agency outcomes for some medicine/patient population pairings in the study sample were pending at this time.

Close attention was paid to ensure the patient population for a given pairing was consistent across all agencies; a small number of assumptions were required.

Adjustments were made for the outcomes made by IQWiG/G-BA and the TC to align them with the PBAC's outcome categories (i.e. recommendation, rejection, deferral; see Appendix).

The following study metrics were used:

- Medicine/patient population pairing considered by the agency (Yes/No)
- Agency outcome/s

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- Time from the date of local registration to the date of final/most recent local HTA agency outcome

Information on HTA agency outcomes were obtained from their respective websites. Local registration dates were obtained from the HTA agency website and/or local regulatory agency website.

Insofar as the dates of submissions to NICE, IQWiG/G-BA and the TC are not in the public domain, it was not possible to determine the mean time from the date of local HTA agency submission to date of final/most recent local HTA agency outcome. It is worthwhile noting that some of the HTA agencies in the study sample do not receive/accept resubmissions.

The PBAC considered 90 discrete cancer medicine/patient populations during the study period. There appears to have been an increase over time in the number of cancer medicine/patient populations being considered by the PBAC on an annual basis. A greater proportion of the pairings from the earlier years of the study period have been resolved (e.g. the most recent PBAC outcome is a recommendation).

Twelve of the 90 pairings are unique to Australia. None of the other HTA agencies had issued a final outcome for all of the remaining 78 pairings as at 1 October 2016. 22 of the 30 PBAC rejected medicine/patient population pairings have a 'positive' final outcome from at least one other HTA agency. Some of these pairings also have a 'negative' final outcome from another HTA agency. The following eight PBAC rejected pairings have multiple 'positive' HTA agency outcomes, suggesting the PBAC may be applying a more stringent standard than several of its peer agencies:

- Abiraterone acetate for patients with advanced/metastatic, castration-resistant prostate cancer (later-line) (NICE, IQWiG, TC)
- Brentuxumab vedotin for patients with CD30 positive, relapsed/refractory Hodgkin's lymphoma (pCERC, IQWiG, TC)
- Regorafenib monohydrate for patients with advanced/metastatic gastro-intestinal stromal tumour (pCERC, IQWiG, TC)
- Ponatinib hydrochloride with treatment resistant acute lymphoblastic leukaemia (pCERC, IQWIG, TC)
- Afatinib dimaleate for patients with advanced metastatic colorectal cancer (later-line) (pCERC, NICE, IQWiG, TC)
- Enzalutamide for patients with advanced/metastatic, castration-resistant prostate cancer (first-line) (pCERC, NICE, IQWiG, TC)
- Nivolumab for patients with advanced/metastatic, squamous cell lung cancer (later-line) (pCERC, IQWiG, TC)
- Olaparib for patients with advanced/metastatic ovarian cancer (later-line) (NICE, IQWiG, TC)

Of the 60 PBAC recommended pairings, there are no examples where there is a final outcome for all of the other HTA agencies and they are all 'negative'.

The results for the time to event analysis indicate a much longer period for then PBAC (mean of 412 days) when compared with the results for the other HTA agencies (mean of 150 – 272 days). It is important to note that these are mean values and as such 'hide' extreme values.

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 goal.

The objective of the project was to update the 2014 analysis of submissions for new medicines for patients with cancer to the Pharmaceutical Benefits Advisory Committee (PBAC) and other comparable health technology assessment (HTA) agencies.

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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 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 meeting; relevant initial submissions from the July 2016 meeting were not considered.

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

- Cetuximab (Erbitux) for metastatic colorectal cancer (advanced/metastatic, KRAS wild type)

- Everolimus (Afinitor) for renal cell carcinoma
- Panitumumab (Vectibix) for colorectal cancer (advanced/metastatic, KRAS wild type, second-line)
- 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.

Comparisons were made with following health technology assessment (HTA) agencies:

- The Pan Canadian Oncology Drug Review (pCODR) Expert Review Committee (pCERC) in Canada. The pCERC has only been in existence since late 2011.
- The National Institute of Health and Care Excellence (NICE) in England
- The Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care; IQWiG) and the Gemeinsamer Bundesausschuss (G-BA) in Germany. The IQWiG seldom assessed new medicines for patients with cancer before the AMNOG reforms that were introduced in 2011.
- The Transparency Commission (TC) in France

These agencies are explained in more details in the Appendix.

The following data were collected for each medicine/patient population pairing for each HTA agency:

- Date of registration – Australia (Therapeutic Goods Administration), Europe (European Commission) and Canada (Health Canada)
- Date/s of submission/s (if available)
- Number of submissions (if relevant)
- Date/s of outcome/s
- Outcome/s (i.e. recommended, not/recommended, deferred, unresolved)

Data were aggregated for each calendar year in the study period as well as for the cumulative study period (calendar year = calendar year of most recent PBAC outcome).

The analysis captures HTA agency outcomes up and including 1 October 2016. Final HTA agency outcomes for some medicine/patient population pairings in the study sample were pending at this time.

It is important to note the processes and operations of the various HTA agencies. While NICE, IQWIG and the Transparency Commission initiate the assessment process, the assessment process in Canada and Australia is initiated by the applicant/sponsor. In the case of the former, the assessment process will be

determined to a large part by regulatory outcome timelines; commercial considerations will have a greater bearing for the latter.

Furthermore, while some HTA agencies (e.g. IQWiG) determine the patient population/s for assessment, others (e.g. PBAC) respond to the patient population/s proposed by the applicant/sponsor. The IQWiG/G-BA has a propensity to create unique patient populations (sub-groups) (i.e. patient population/s that are not specified in a medicine's Summary of Product Characteristics and have not been created elsewhere).

The following study metrics were used:

- Medicine/patient population pairing considered by the agency (Yes/No)
- Agency outcome/s (some agencies do not issue 'recommendations' *per se*)
- Time from the date of local registration to the date of final/most recent local HTA agency outcome

The following assumptions were made regarding submission and outcome dates for the following HTA agencies.

IQWiG

- Submission dates are not available
- The date of the IQWiG assessment report was deemed to be the outcome date
- The outcome from an IQWiG appendix was used if it was different to the initial IQWiG outcome
- The IQWiG does not subject orphan medicines to a full assessment if their annual expenditure remains below a threshold level. Some orphan medicines have exceeded the threshold and were subjected to a full assessment at a later date. These outcomes were not considered.
- Insofar as the G-BA is more a 'decision-maker' than a 'HTA agency'; its outcomes have generally not been considered

NICE

- Submission dates are not available
- The date of the last Appraisal Committee meeting was deemed to be outcome date
- Only the outcome from an initial assessment/appraisal was used; an outcome from a scheduled review of a previous technology assessment was not considered

pCERC

- Submission dates are generally available
- Submissions can be lodged pre-registration (a pre Notice of Compliance or 'pre-NoC submission')
- The date of the final recommendation was deemed to be the outcome date
- Dates and outcomes for resubmissions were used over those for initial submissions (if applicable)

TC

- Submission dates are not available
- The date of an opinion was deemed to be the outcome date
- Only the outcome from an initial assessment/appraisal was used; an outcome from a scheduled review of a previous opinion was not considered

The IQWiG and the TC do not issue outcomes in the same/similar manner as the PBAC, NICE and the pCERC; their outcomes are expressed in terms of the level/degree of the additional clinical benefit. Appendix A describes the approach taken to align the IQWiG and TC outcomes to those of the other agencies. The approach taken could be argued to be biased in the direction of increasing the number of positive outcomes from these two agencies. However, the approach was taken on the assumption that the ratings counted as positive outcomes could still result in subsidised access, whereas a rejection by the other agencies clearly does not allow this. We believe this assumption is reasonable.

RESULTS

The PBAC considered 90 discrete cancer medicine/patient populations during the study period (Table 1).

Table 1 – Medicine/patient population pairings

Calendar year	Number of medicine/patient population pairings
2010	5
2011	5
2012	6
2013	14
2014	15
2015	26
2016	19
Total	**90**

The results in Table 1 suggest an increase in the number of cancer medicine/patient populations being considered by the PBAC over time. A firm conclusion cannot be made due to the exclusion of resubmissions that were considered by the PBAC in 2010 and 2011. Nonetheless, the number of exclusions for 2010 and 2011 are not high (data not shown).

Some of the medicine/patient population pairings in the study sample are unique to Australia.

The medicine/patient population pairings for 2010 are presented in Table 2. The number of pairings is small. Insofar as the AMNOG reforms were yet to implemented in Germany and the pan Canadian Oncology Drug Review process had not been established; there are not that many outcomes for the other four HTA agencies.

There are no apparent issues with the matching of patient populations.

Table 2 – HTA agency outcomes for 2010 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	pCERC	NICE	IQWiG	TC
Bortezomib	Multiple myeloma	Newly diagnosed, combination, ineligible for high dose chemotherapy	Reject	No assessment	No assessment	No assessment	No assessment
Rituximab	Chronic lymphocytic leukaemia	CD20 positive, first-line, combination	Recommend	No assessment	Recommend (NICE)	No assessment	Important, IV
Degarelix acetate	Prostate cancer	Advanced/metastatic	Recommend	No assessment	No assessment	No assessment	Important, V
Topotecan hydrochloride	Small-cell lung cancer	Relapsed, monotherapy	Reject	No assessment	Recommend (NICE)	No assessment	Important, IV
Bevacizumab	Brain cancer	Advanced/metastatic, relapsed/progressive, later-line, monotherapy	Reject	No assessment	Approved (CDF)	No assessment	No assessment

Five medicine/patient population pairings were considered by the PBAC for the last time in 2010 (more were considered in 2010 but they were also considered in previous and/or subsequent years). Two of the five pairings were (ultimately) recommended and the other three remain rejected.

None of the five medicine/patient population pairings have been considered by the Canadian and German HTA agencies.

The two medicine/patient population pairings (ultimately) recommended by the PBAC were also 'recommended' by NICE (rituximab) and the Transparency Commission (rituximab and degarelix acetate).

While the PBAC rejected the submission for **oral** topotecan hydrochloride for patients with small-cell lung cancer due to uncertain clinical benefit, it was 'recommended' by NICE (without a patient access scheme) and by the Transparency Commission (with an ASMR rating of IV, which indicates the Commission was of the view that it has some additional clinical benefit).

It is important to note that the PBAC submission for topotecan hydrochloride sought a listing for the oral capsules as a treatment option for patients with relapsed small-cell lung cancer for whom second-line intravenous chemotherapy is inappropriate. The submission did not seek to replace intravenous form of topotecan hydrochloride that was not PBS listed for use by patients with small-cell lung cancer.

Bevacizumab was approved for listing in the Cancer Drugs Fund. In November 2008, the Department of Health asked NICE to conduct an appraisal of bevacizumab for the treatment of patients with recurrent glioblastoma and to provide guidance on its use to the NHS in England and Wales.

In 2009, NICE noted that the EMA CHMP had adopted a negative opinion on extending the current indication of bevacizumab to include its use in patients with recurrent glioblastoma; the agency therefore decided to remove the appraisal for

bevacizumab for brain cancer from its work programme. Bevacizumab is currently not registered in Europe for use by patients with brain cancer.

The medicine/patient population pairings for 2011 are presented in Table 3. The number of pairings is small. Insofar as the AMNOG reforms had just been implemented in Germany and the pan Canadian Oncology Drug Review process had not been established; there are not that many outcomes for the other four HTA agencies.

There are no apparent issues with the matching of patient populations.

Table 3 – HTA agency outcomes for 2011 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	pCERC	NICE	IQWiG	TC
Bevacizumab	Non-small-cell lung cancer	Advanced/metastatic	Reject	No assessment	No assessment	No assessment	Important, V
Vorinostat	Non-Hodgkin's lymphoma	Cutaneous T-cell lymphoma, advanced, refractory/resistant	Reject	No assessment	No assessment	No assessment	No assessment
Bortezomib	Multiple myeloma	Newly diagnosed, renal failure, later-line	Recommend	No assessment	No assessment	No assessment	No assessment
Dasatinib monohydrate	Chronic myeloid leukaemia	Chronic phase, newly diagnosed, first-line	Recommend	No assessment	Rejection	No assessment	No assessment
Nilotinib hydrochloride monohydrate	Chronic myeloid leukaemia	Chronic phase, newly diagnosed, first-line	Recommend	No assessment	Recommend	No assessment	Important, IV

Five medicine/patient population pairings were considered by the PBAC for the last time in 2011. Three of the five pairings were (ultimately) recommended and the other two remain rejected.

None of the five medicine/patient population pairings have been considered by the Canadian and German HTA agencies.

Only one of the three medicine/patient population pairings has been considered by another HTA agency; nilotinib hydrochloride monohydrate was 'recommended' by the Transparency Commission with an ASMR rating of IV.

The PBAC rejected the one and only submission for bevacizumab for use by certain patients with non-small-cell lung cancer on the basis of uncertain cost-effectiveness. It was considered by considered by only one other HTA agency (Transparency Commission) and was 'recommended' with an ASMR rating of V. The Transparency Commission reviewed the reimbursement of bevacizumab for use by patients with non-small-cell lung cancer in 2016; the SMR & ASMR ratings remain unchanged.

To date, the PBAC has only considered one submission for vorinostat for patients with cutaneous T-cell lymphoma; it was rejected because the proposed main comparator was incorrect. The PBAC will consider a resubmission for vorinostat in

November 2016. Vorinostat is yet to be considered by the other HTA agencies; ostensibly because it is not registered in Canada and Europe.

The medicine/patient population pairings for 2012 are presented in Table 4.

There are no apparent issues with the matching of patient populations.

Table 4 – HTA agency outcomes for the 2012 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	pCERC	NICE	IQWiG	TC
Bortezomib	Multiple myeloma	Newly diagnosed, combination, eligible for high dose chemotherapy	Recommend	No assessment	No assessment	No assessment	No assessment
Cabazitaxel	Prostate cancer	Advanced/metastatic, hormone refractory, later-line, combination	Recommend	No assessment	Reject	Significant/Marginal	Important, III
Pazopanib hydrochloride	Renal cell carcinoma	Stage IV clear cell variant, newly diagnosed, first-line	Recommend	Recommend	Recommend	No assessment	Low, V
Trastuzumab	Breast cancer	Early, HER2 positive, neo-adjuvant, combination	Recommend	No assessment	No assessment	No assessment	Important, IV
Abiraterone acetate	Prostate cancer	Advanced/metastatic, castration-resistant, later-line, combination	Recommend	Recommend	Recommend	Significant	Important, III
Ipilimumab	Malignant melanoma	Unresectable, first-line	Recommend	Recommend	Recommend	No assessment	Important, IV

Six medicine/patient population pairings were considered by the PBAC for the last time in 2012; all six were (ultimately) recommended.

Of the six medicine/patient population pairings:

- Three have been considered by the pCERC; all three were recommended
- Four have been considered by NICE, of which three were recommended. The rejected medicine/patient population (cabazitaxel for patients with advanced/metastatic, hormone refractory prostate cancer) was later approved for listing in the Cancer Drugs Fund.
- Two have been considered by the IQWiG in Germany and found to have some additional clinical benefit. The degree of additional clinical benefit for one medicine/patient population (cabazitaxel) was later downgraded by the G-BA.
- Five have been considered by the Transparency Commission in France and were all 'recommended' for reimbursement. Four of the five pairings were deemed to have an additional clinical benefit; the other medicine/patient population pairing (pazopanib hydrochloride for patients with sarcoma) was deemed to have an SMR rating of low and no additional clinical benefit (ASMR rating of V). Interestingly, the initial ASMR rating for cabazitaxel was IV; it was later upgraded to III.

The medicine/patient population pairings for 2013 are presented in Table 5.

There are no apparent issues with the matching of patient populations.

While the PBAC had previously considered a submission for panitumumab for use by patients with colorectal cancer, it had not considered its use in combination with

chemotherapy for the **first-line** treatment of patients with **KRAS wild type** advanced/metastatic disease. This issue became redundant as the Product Information for panitumumab was revised in 2014 to confine its use to patients with **RAS wild type** disease.

Table 5 – HTA agency outcomes for the 2013 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	ERC	NICE	IQWiG	TC
Lenalidomide	Myelodysplastic syndrome	5q cytogenetic abnormality, low or intermediate-1 grade disease	Recommend	No assessment	Recommend	No assessment	Important, III
Panitumumab	Colorectal cancer	Advanced/metastatic, K-RAS wild type, first-line, combination	Reject	No assessment	No assessment	No assessment	Important, V
Vinorelbine tartrate	Breast cancer	Advanced/metastatic, later-line, monotherapy	Recommend	No assessment	Recommend	No assessment	Important, V
Vinorelbine tartrate	Breast cancer	Advanced/metastatic, later-line, combination	Recommend	No assessment	Recommend	No assessment	Important, V
Everolimus	Tuberous sclerosis complex	Subependymal giant cell	Recommend	No assessment	No assessment	No assessment	Important, II
Dabrafenib mesylate	Malignant melanoma	Unresectable, BRAF V600 mutation positive	Recommend	Recommend	Recommend	No benefit	Important, V
Pazopanib hydrochloride	Sarcoma	Advanced/metastatic	Recommend	No assessment	No assessment	No assessment	Important, IV
Aflibercept	Colorectal cancer	Advanced/metastatic, later-line, combination	Reject	Reject	Reject	Marginal	Important, V
Erlotinib hydrochloride	Non-small-cell lung cancer	Advanced/metastatic, activating EGFR gene mutation positive, first-line	Recommend	No assessment	Recommend	No assessment	Important, IV
Gefitinib	Non-small-cell lung cancer	Advanced/metastatic, activating EGFR gene mutation positive, first-line, monotherapy	Recommend	No assessment	Recommend	No assessment	Important, V
Gefitinib	Non-small-cell lung cancer	Advanced/metastatic, activating EGFR gene mutation positive, first-line, monotherapy, maintenance	Recommend	No assessment	No assessment	No assessment	No assessment
Sunitinib maleate	Pancreatic neuroendocrine tumour	Unresectable, well-differentiated	Recommend	No assessment	No assessment	No assessment	Moderate, V
Everolimus	Breast cancer	Advanced/metastatic, combination	Recommend	No assessment	Reject	No assessment	Low, V
Eribulin mesylate	Breast cancer	Advanced/metastatic, third-line	Recommend	Recommend	Reject	Non quantifiable	Important, IV

Fourteen medicine/patient population pairings were considered by the PBAC for the last time in 2013; twelve were (ultimately) recommended.

Of the 14 medicine/patient population pairings:

- Only three have been considered by the pCERC in Canada of which two were recommended

- Nine have been considered by NICE of which six were recommended. The use of everolimus on the NHS for patients with breast cancer was rejected by NICE but was later approved for listing in the Cancer Drugs Fund. Its listing in the Fund is currently under review by NICE.
- Three have been considered by the IQWiG
- Twelve have been considered by the Transparency Commission in France. Sunitinib maleate for use by patients with a pancreatic neuroendocrine tumour received an SMR rating of moderate (ASMR rating of V) and everolimus for use by patients with breast cancer received an SMR rating of low (ASMR rating of V).

The sole PBAC rejection was for aflibercept for use by patients with advanced/metastatic colorectal cancer; while it was 'recommended' for reimbursement by the IQWiG in Germany and by the Transparency Commission in France, it was rejected by the pCERC in Canada and NICE in England.

The medicine/patient population pairings for 2014 are presented in Table 6.

There is an issue with the matching of patient populations for trametinib dimethyl sulphoxide.

The IQWiG assessed the additional clinical benefit of trametinib dimethyl sulphoxide when used in combination with dabrafenib mesylate by way of gender. The initial assessment found a higher level of additional benefit in women (major versus non quantifiable), the supply of additional data in an appendix resulted the rating for men being changed to significant/considerable.

Table 6 – HTA agency outcomes for the 2014 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	pCERC	NICE	IQWiG	TC
Bevacizumab	Ovarian cancer	Advanced epithelial ovarian, fallopian tube or primary peritoneal cancer, first-line, combination	Recommend	No assessment	Reject	No assessment	Important, IV
Brentuximab vedotin	Non-Hodgkin's lymphoma	Anaplastic large cell, relapsed/refractory	Recommend	Recommend	No assessment	No assessment	Important, III
Everolimus	Pancreatic neuroendocrine tumour	Unresectable, well-differentiated	Recommend	Recommend	No assessment	No assessment	Important, IV
Paclitaxel (nanoparticle albumin bound)	Pancreatic cancer	Advanced/metastatic, combination	Recommend	Recommend	Reject	No assessment	Important, IV
Enzalutamide	Prostate cancer	Advanced/metastatic, castration-resistant, later-line	Recommend	Recommend	Recommend	Significant	Important, III
Abiraterone acetate	Prostate cancer	Advanced/metastatic, castration-resistant, later-line	Reject	No assessment	Recommend	Significant	Important, IV
Regorafenib monohydrate	Colorectal cancer	Advanced/metastatic, later-line	Reject	Reject	No assessment	No benefit	Low, V
Axitinib	Renal cell carcinoma	Stage IV clear cell variant, later-line	Recommend	Recommend	Recommend	Significant	Important, IV
Cetuximab	Colorectal cancer	Advanced/metastatic, RAS wild type, first-line	Recommend	No assessment	No assessment	No assessment	No assessment
Crizotinib	Non-small-cell lung cancer	Advanced/metastatic, anaplastic lymphoma kinase positive, later-line	Recommend	Recommend	Reject	No benefit	Important, III
Ofatumumab acetate	Chronic lymphocytic leukaemia	CD20 positive, treatment naïve, combination	Recommend	Reject	Recommend	No assessment	Important, V
Pomalidomide	Multiple myeloma	Relapsed/refractory, combination	Recommend	Recommend	Reject	No benefit	Important, III
Trametinib dimethyl sulphoxide	Malignant melanoma	Advanced/metastatic, BRAF V600 mutation positive, combination	Recommend	No assessment	Recommend	Major (significant)	Important, III
Pertuzumab	Breast cancer	Advanced/metastatic, HER2 positive, combination	Recommend	Recommend	Pending	Significant	Important, III
Trastuzumab emtansine	Breast cancer	Advanced/metastatic, HER2 positive, later-line	Recommend	Recommend	Reject	Major	Important, II

Fifteen medicine/patient population pairings were considered by the PBAC for the last time in 2014; thirteen were (ultimately) recommended.

Of the sixteen medicine/patient population pairings:

- Eleven have been considered by the pCERC in Canada, of which nine were recommended
- Ten have been considered by the NICE, of which five were rejected. All five were later approved for listing in the Cancer Drugs Fund. The assessment of pertuzumab for patients with breast cancer by NICE is on-going; draft guidance has recommended rejection.

- Eight have been considered by the IQWiG in Germany. The IQWiG assessed the benefits trametinib dimethyl sulphoxide by way of gender; the IQWiG initially found a differential benefit between men and women, but this was subsequently revised upon the supply of additional data.
- Fourteen have been considered by the Transparency Commission.

The two PBAC rejected medicine/patient population pairings are panitumumab for patients with KRAS wild-type colorectal cancer and regorafenib monohydrate for advanced/metastatic colorectal cancer. The former pairing has only been considered by one other agency (Transparency Commission), whereas the latter has been assessed by four other agencies. The assessment of regorafenib monohydrate by these agencies was generally not that favourable, insofar as it was rejected by the pCERC in Canada and the Transparency Commission gave it an SMR rating of low.

The Transparency Commission subsequently reviewed its initial ASMR rating for abiraterone acetate; the rating remained unchanged.

The medicine/patient population pairings for 2015 are presented in Table 7.

There are issues with the matching of the patient populations for pembrolizumab and afatinib dimaleate.

The PBAC recommended the reimbursement of pembrolizumab for use by patients with unresectable malignant melanoma who are ipilimumab naïve. Other HTA agencies considered the merits of pembrolizumab in patients who are treatment naïve (i.e. first-line). Insofar as some patients may have been treated with other medicines (e.g. dacarbazine) before the use of ipilimumab naïve, they are not the same. Given the benefits of dacarbazine in these patients are modest, its use is in decline. For the purposes of this analysis, it has ben assumed that patients who are ipilimumab naïve are treatment naïve.

In 2013, the PBAC considered the reimbursement of afatinib dimaleate for use by patients with advanced/metastatic non-small-cell lung cancer with an endothelial growth factor receptor (EGFR) mutation. The Committee recommended afatinib dimaleate for first–line use but rejected its use for second and subsequent lines. The recommendation did not result in a PBS listing. In 2015, the PBAC considered the listing of afatinib dimaleate for use by patients with advanced/metastatic non-small-cell lung cancer with a **specific** endothelial growth factor receptor (EGFR) mutation (exon 19 deletion mutation; Del19 mutation). There are many EGFR mutations; the Del19 mutation is said to be a common one (frequency of approximately 48% in EGFR mutated lung tumours).

The German IQWiG considered the reimbursement of afatinib dimaleate for use by patients with other EGFR mutations such as the L858R mutation, as well as the Del19 mutation. For the purposes of this analysis, it has been assumed that patients with an L858R mutation or a Del19 mutation are the same as patients who have an unspecified EGFR mutation.

The IQWiG considered the reimbursement of nivolumab for use by patients with malignant melanoma in terms of gender. While the agency found there are additional clinical benefits in both men and women, it found a greater benefit in men. The other HTA agencies did not examine the benefits of nivolumab by way of gender.

The IQWiG considered the reimbursement of enzalutamide for use by male patients with prostate cancer in terms of age. While the agency found there are additional clinical benefits in both younger (<75 years) and older (>75 years) men, it found a greater benefit in older men. The other HTA agencies did not examine the benefits of nivolumab by way of age.

Table 7 – HTA agency outcomes for the 2015 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	pCERC	NICE	IQWiG	TC
Obinutuzumab	Chronic lymphocytic leukaemia	CD20 positive, treatment naïve, combination (chlorambucil)	Recommend	Recommend	Recommend	Not quantifiable	Important, III
Panitumumab	Colorectal cancer	Advanced/metastatic, RAS wild type, first-line, combination (FOLFOX)	Recommend	No assessment	No assessment	No assessment	Important, IV
Pembrolizumab	Malignant melanoma	Unresectable, ipilimumab naïve	Recommend	Recommend	Recommend	Not quantifiable	Important, V
Ruxolitinib phosphate	Myelofibrosis	Idiopathic	Recommend	Recommend	Recommend	Significant	Important, III
Ruxolitinib phosphate	Myelofibrosis	Polycythemia vera	Recommend	Recommend	Recommend	Significant	Important, III
Ruxolitinib phosphate	Myelofibrosis	Essential thrombocythemia	Recommend	Recommend	Recommend	Significant	Important, III
Bendamustine hydrochloride	Non-Hodgkin's lymphoma	Indolent, relapsed/refractory (rituximab)	Reject	Recommend	No assessment	No assessment	Important, III
Bendamustine hydrochloride	Non-Hodgkin's lymphoma	Indolent, first-line	Recommend	Recommend	No assessment	No assessment	No assessment
Bendamustine hydrochloride	Non-Hodgkin's lymphoma	Mantle cell, first-line	Recommend	Recommend	No assessment	No assessment	No assessment
Brentuximab vedotin	Hodgkin's lymphoma	CD30 positive, relapsed/refractory, later-line	Reject	Recommend	No assessment	Not quantifiable	Important, III
Regorafenib monohydrate	Gastro-intestinal stromal tumour	Advanced/metastatic, later-line	Reject	Recommend	No assessment	Not quantifiable	Important, IV
Ponatinib hydrochloride	Chronic myeloid leukaemia	Treatment resistant (dasatinib monohydrate and nilotinib hydrochloride monohydrate)	Recommend	Recommend	No assessment	Not quantifiable	Important, V

Ponatinib hydrochloride	Chronic myeloid leukaemia	T315I mutation positive	Recommend	Recommend	No assessment	Not quantifiable	Important, III
Ponatinib hydrochloride	Acute lymphoblastic leukaemia	T315I mutation positive	Recommend	Recommend	No assessment	Not quantifiable	Important, IV
Ponatinib hydrochloride	Acute lymphoblastic leukaemia	Treatment resistant (dasatinib monohydrate and nilotinib hydrochloride monohydrate)	Reject	Recommend	No assessment	Not quantifiable	Important, V
Trastuzumab	Gastric cancer	Advanced/metastatic, HER2 positive, first-line, combination	Recommend	No assessment	Recommend	No assessment	Important, IV
Afatinib dimaleate	Non-small-cell lung cancer	Advanced/metastatic, activating, EGFR Del19 mutation, later-line	Reject	Recommend	Recommend	Major	Important, V
Afatinib dimaleate	Non-small-cell lung cancer	Advanced/metastatic, activating EGFR Del19 mutation, first-line	Reject	No assessment	No assessment	Pending	No assessment
Nivolumab	Malignant melanoma	Unresectable, later-line	Recommend	Recommend	Recommend	Major (Significant)	Important, III
Nivolumab	Malignant melanoma	Unresectable, first-line, combination (ipilimumab)	Reject	No assessment	Recommend	No assessment	No assessment
Ipilumumab	Malignant melanoma	Unresectable, first-line, combination (nivolumab)	Reject	No assessment	Recommend	No assessment	No assessment
Sorafenib tosylate	Thyroid cancer	Papillary or follicular thyroid carcinoma, advanced/metastatic	Reject	Reject	No assessment	No assessment	Important, IV
Arsenic trioxide	Acute promyelocytic leukaemia	Newly diagnosed, induction	Recommend	No assessment	No assessment	No assessment	No assessment
Enzalutamide	Prostate cancer	Advanced/metastatic, castration-resistant, first-line	Reject	Recommend	Recommend	Significant (Major)	Important, V
Lanreotide acetate	Pancreatic neuroendocrine tumour	Advanced/metastatic	Reject	No assessment	No assessment	No assessment	Important, V
Vinflunine ditartrate	Urinary tract cancer	Transitional cell carcinoma, advanced/metastatic, later-line	Reject	No assessment	Reject	No assessment	Moderate, V

26 medicine/patient population pairings were considered by the PBAC for the last time in 2015; 14 were (ultimately) recommended.

Of the twelve rejected medicine/patient population pairings, six were considered by two or more HTA agencies:

- Regorafenib monohydrate was 'recommended' by the pCERC, IQWiG and the TC
- Ponatinib hydrochloride was 'recommended' for use by patients with treatment resistant acute lymphoblastic leukaemia by the pCERC, IQWiG and the TC
- Afatinib dimaleate was 'recommended' for first-line use by the pCERC, NICE, IQWiG and the TC. Its use for second (and later) line use is yet to be considered by the other HTA agencies.
- Sorafenib tosylate was 'recommended' for use by patients with thyroid cancer by the TC but rejected by the pCERC
- Enzalutamide was 'recommended' for first-line use by the pCERC, NICE, IQWiG and the TC
- Vinflunine tartrate was 'recommended' by the TC (with an SMR rating of 'moderate' rather than 'important') but was rejected by the pCERC

The Transparency Commission rated lanreotide acetate as being important with an ASMR of V for patients with an unresectable locally advanced or metastatic gastro-enteropancreatic neuroendocrine tumour that is not progressive. For patients with progressive disease, it was rated lower (SMR = insufficient).

The medicine/patient population pairings for 2016 are presented in Table 8.

There are issues with the matching of patient populations for ibrutinib, idelalisib and nivolumab.

The respective pivotal clinical trials for the kinase inhibitors ibrutinib and idelalisib included patients with chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL); the RESONATE trial for ibrutinib and the 312-0116 trial for idelalisib. CLL and SLL are discrete diseases; small lymphocytic lymphoma is classified as a non-Hodgkin's lymphoma and is distinct from indolent non-Hodgkin's lymphoma.

While the PBAC has considered submissions to consider both of these medicines for both diseases, the other HTA agencies have only considered their reimbursement for patients with chronic lymphocytic leukaemia.

Idelalisib and ibrutinib can be used as first-line treatments in patients with certain mutations (17p deletion mutation and TP53 mutation). The PBAC did not consider the reimbursement of these medicines for these patients in the study period.

The IQWiG has investigated the benefits of nivolumab in patients with non-small-cell lung cancer in unique sub-groups.

For non-squamous cell lung cancer, the effects of nivolumab have been examined by way of the patients' eligibility to be treated with further chemotherapy. The agency determined there is a differential benefit.

For squamous cell lung cancer, the effects of nivolumab have been examined by way of the patients' baseline age and health status. The agency determined there is a differential benefit.

Table 8 – HTA agency outcomes for the 2016 medicine/patient population pairings

Medicine	Disease	Patient population	PBAC	pCERC	NICE	IQWiG	TC
Bevacizumab	Cervical cancer	Advanced/metastatic, combination	Recommend	Recommend	No assessment	No assessment	No assessment
Ibrutinib	Chronic lymphocytic leukaemia	Later-line	Reject	Pending	Pending	Not quantifiable	Important, III
Ibrutinib	Non-Hodgkin's lymphoma	Small lymphocytic lymphoma, later-line	Reject	No assessment	No assessment	No assessment	No assessment
Idelalisib	Chronic lymphocytic leukaemia	Relapsed, combination (rituximab)	Recommend	Recommend	Recommend	No benefit	Important, III
Idelalisib	Non-Hodgkin's lymphoma	Small lymphocytic lymphoma, later-line	Recommend	No assessment	No assessment	No assessment	No assessment
Idelalisib	Non-Hodgkin's lymphoma	Indolent, later-line	Recommend	Recommend	No assessment	No benefit	Important, IV
Nivolumab	Non-small-cell lung cancer	Non-squamous cell, advanced/metastatic, later-line	Reject	Recommend	No assessment	Significant (no additional benefit)	No assessment
Nivolumab	Non-small-cell lung cancer	Squamous cell, advanced/metastatic, later-line	Reject	Recommend	Pending	Major (non quantifiable, no additional benefit)	Important, III
Olaparib	Ovarian cancer	Advanced/metastatic, later-line, monotherapy	Reject	Reject	Recommend	Not quantifiable	Important, IV
Lenvatinib mesylate	Thyroid cancer	Advanced/metastatic, later-line	Recommend	Recommend	No assessment	Not quantifiable	Important, IV
Lenalidomide	Multiple myeloma	Newly diagnosed, combination	Recommend	No assessment	No assessment	No assessment	No assessment
Vemurafenib	Malignant melanoma	Unresectable, BRAF V600 mutation positive, combination (cobimetinib hemifumarate)	Recommend	Recommend	Recommend	Significant	Important, III
Tamoxifen citrate	Breast cancer	Primary prevention	Recommend	No assessment	No assessment	No assessment	No assessment
Cetuximab	Head and neck cancer	Advanced/metastatic, combination (platinum-based chemotherapy)	Reject	No assessment	Reject	No assessment	Important, III
Cobimetinib hemifumarate	Malignant melanoma	Unresectable, BRAF V600 mutation positive, combination (vemurafenib)	Recommend	Recommend	No assessment	Significant	Important, III
Nintedanib esylate	Non-small-cell lung cancer	Advanced/metastatic, later-line, combination	Reject	No assessment	Recommend	Marginal	Insufficient, VI

Vismodegib	Basal cell carcinoma	Advanced/metastatic	Recommend	Recommend	No assessment	No benefit	Important, IV
Blinatumomab	Acute lymphoblastic leukaemia	B-cell, relapsed/refractory	Recommend	Reject	Pending	Pending	Important, III
Pralatrexate	Non-Hodgkin's lymphoma	T-cell, relapsed/refractory	Reject	No assessment	No assessment	No assessment	No assessment

Nineteen medicine/patient population pairings were considered by the PBAC for the last time in 2016; eleven were (ultimately) recommended.

Of the nineteen rejected medicine/patient population pairings, six have been considered by two or more HTA agencies:

- Ibrutinib was 'recommended' for use by patients with chronic lymphocytic leukaemia by the IQWIG and the TC
- Nivolumab was 'recommended' for use by patients with non-squamous cell lung cancer by the pCERC and IQWiG
- Nivolumab was 'recommended' for use by patients with squamous cell lung cancer by the pCERC, IQWiG and the TC
- Olaparib was 'recommended' for use by patients with ovarian cancer by NICE, IQWiG and the TC but was rejected by the pCERC
- Cetuximab was 'recommended' for use by patients with head and neck cancer by the TC but was rejected by the pCERC
- Nintedanib esylate was 'recommended' for use by patients with non-small-cell lung cancer by NICE and the IQWiG but was rejected by the TC

Time to event analysis

Ninety medicine/patient population pairings were considered for the analysis (Table 1).

The results presented above in Tables 2-8 indicate that the IQWIG, NICE, pCERC and the TC have not (yet) assessed all 90 pairings. Twelve of the 90 pairings are unique to Australia (Table 9).

Table 9 – Medicine/patient population pairings unique to Australia

Year	Medicine
2010	Bortezomib
2011	Vorinostat, Bortezomib
2012	Bortezomib
2013	Gefitinib
2014	Cetuximab
2015	Afatinib dimaleate
2016	Idelalisib, Ibrutinib, Lenalidomide, Tamoxifen citrate, Pralatrexate

It was decided *a priori* that the final study sample for this analysis would be comprised of the pairings that have been considered by the PBAC and at least one other HTA agency, regardless of the PBAC's (or other agency's) final outcome.

Accordingly, the medicines cited in Table 9 were excluded from the analysis. The resultant study sample is therefore 78 medicine/patient population pairings.

The primary objective was to determine the mean period (in days) from the date of local registration to the date of the last HTA agency outcome for each pairing for each agency.

Information on the sourcing of local registration dates in provided in Table 10.

Table 10 – Sourcing of local registration dates

HTA agency	Source/s of local registration dates	Comment
PBAC	PBS website (PBAC Public Summary Document), TGA website (Product Information, Australian Public Assessment Report)	ARTG start date (new medicine), Date of decision (new indication)
IQWiG	EMA website (Authorisation details)	Date of approval by the European Commission
NICE	EMA website (Authorisation details)	Date of approval by the European Commission
pCERC	CADTH website (Agency report summary), Health Canada website	Date of Notice of Compliance (NoC date)
TC	EMA website (Authorisation details)	Date of approval by the European Commission

Information on the date of the last outcome for each HTA agency is provided in Table 11.

Table 11 – Last HTA agency outcome for a given medicine/patient population pairing

HTA agency	Last outcome	Comment
PBAC	Date of most recent PBAC meeting	Date of outcome of resubmission (if applicable)
IQWiG	Date of assessment report	G-BA outcome dates not considered
NICE	Date of most recent Appraisal Committee meeting	Appeal dates not considered
pCERC	Date of final recommendation	Date of outcome of resubmission (if applicable)

TC	Date of opinion	

Insofar as submission dates are not available for the IQWIG, NICE and the TC, analyses to determine the period from the date of local registration to the date of the local HTA agency submission or the period from the date of local HTA agency submission to the date of local HTA agency outcome were not attempted.

This metric has both merits and demerits. Its merits are:

- It is metric of 'market access' insofar as it seeks to consider relevant registration and reimbursement outcomes
- It will capture efforts by HTA agencies so consider the reimbursement of a new technology before its local registration. As such, it is possible to have negative values for some HTA agencies.
- Data are in the public domain to enable the determination of values for pairings for all HTA agencies and thus permit a wider comparison

Its demerits are:

- It assumes that the commencement of reimbursement process is closely aligned with the local regulatory process, which may not be the case for all pairings for all HTA agencies. Insofar as the reimbursement process in Australia and Canada is initiated by the sponsor/applicant rather than the HTA agency, there may be instances where the commencement of the reimbursement process may have occurred some after the conclusion of the local registration process. The use of another metric (period from date of initial HTA agency submission to date of local HTA agency outcome would overcome this issue but HTA agency submission dates are not available for the IQWiG, NICE and the TC.

The results for the time to event analysis (period from date of date of local registration to the date of the last HTA agency outcome) are provided in Table 11.

Table 11 – Time to event analysis (period from date of date of local registration to the date of the last HTA agency outcome)

Agency	Period (mean period measured in days; sample size)
PBAC	412 (78)
IQWIG	150 (38)
NICE	272 (41)
pCERC	222 (48)
TC	251 (68)

The results indicate a much longer mean period for the PBAC when compared with the results for the other HTA agencies. It is important to note that these are mean values and as such 'hide' extreme values.

The longer period for the PBAC is due to some or all of the following factors:

- A larger sample size
- HTA agency processes are not exactly the same. The PBAC process commences with a submission from the sponsor/applicant; there are seven PBAC pairings that have a value >1,000 days
- Resubmissions; there are only a few resubmissions in the pCERC sample.
- Number of resubmissions; there are a few pairings with multiple resubmissions.
- 'Local' conditions

A different result may occur with:

- The use of another HTA agency as the control and the PBAC as a test agency
- The requirement for there to be an outcome for two (or more) HTA agencies

Further analysis may be justified to account for entries with extreme values (i.e. period >1,000 days). There are more of these in the PBAC data set:

- Seven for PBAC
- Nil for IQWiG
- Three for NICE
- One for pCERC
- Nil for TC

Extreme values may be due to:

- An extended period between the date of local registration and the date of the **initial** submission (or outcome)
- An extended period between the date of the initial submission (or outcome) and the date of the most recent submission (or outcome)

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 and other comparable HTA agencies 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.

The PBAC considered 90 discrete cancer medicine/patient populations during the study period (2010-2016). There appears to have been an increase in the number of cancer medicine/patient populations being considered by the PBAC over time. A firm conclusion cannot be made due to the exclusion of resubmissions that were considered by the PBAC in 2010 and 2011.

A thorough analysis of the outcomes made by the IQWIG in Germany, NICE in England, pCERC in Canada and the Transparency Commission in France for each medicine in the study sample was undertaken to ensure that the patient population/s closely matched those considered by the PBAC. The patient populations matched up very well in most instances; nonetheless, assumptions were made for a small number of medicines, mostly in the latter years of the study period.

Many of the medicine/patient population pairings in the study sample have not been considered by the other HTA agencies. Of the 90 pairings, only 38 (42%) have been considered by the IQWIG, 41 (46%) by NICE, 48 (53%) by the pCERC and 68% (76%) by the Transparency Commission. Final outcomes for a small number of pairings are pending in England and Canada.

As at 1 October 2016, twelve pairings were unique to the PBAC/Australia. Most, if not all, of these twelve pairings are likely to remain unique for the foreseeable future.

As at 1 October 2016, 60 (67%) of the 90 medicine/patient population pairings had (ultimately) been recommended by the PBAC and 30 (33%) remain rejected.

There are several examples where a given medicine/patient population pairing remains rejected by the PBAC but has been 'recommended' by most/all of the other HTA agencies:

- Abiraterone acetate for patients with advanced/metastatic prostate cancer (later-line) has been 'recommended' by NICE, IQWiG and the TC
- Regorafenib monohydrate for patients with a gastro-intestinal stromal tumour has been 'recommended' by the pCERC, IQWiG and the TC
- Brentuximab vedotin for patients with CD30 positive, relapsed/refractory Hodgkin's lymphoma has been 'recommended' by the pCERC, IQWiG and the TC
- Ponatinib hydrochloride for use by patients with treatment resistant acute lymphoblastic leukaemia has been 'recommended 'by the pCERC, IQWiG and the TC

- Afatinib dimaleate has been ‘recommended’ for first-line use by patients with non-small-cell lung cancer by the pCERC, NICE, IQWiG and the TC. This is a special case insofar as the PBAC recommended the initial submission for afatinib dimaleate for first-line use but rejected the resubmission.
- Enzalutamide has been ’recommended’ for first-line use by patients with prostate cancer by the pCERC, NICE, IQWiG and the TC
- Nivolumab has been ’recommended’ for use by patients with squamous cell lung cancer by the pCERC, IQWiG and the TC
- Olaparib has been ‘recommended’ for use by patients with ovarian cancer by NICE, IQWiG and the TC

The results for the time to event analysis (period from the date of local registration to the date of most recent local HTA agency outcome) indicate a much longer mean period for the PBAC when compared with the results for the other HTA agencies.

The longer period for the PBAC is due to a number of factors, such as having a greater number of parings with extreme values. Further analysis to account/adjust for these pairings should be considered.

APPENDIX

Some renaming and re-classification of agency outcomes was performed to facilitate a meaningful international comparison (Table A).

Table A – Classification of agency outcomes

Agency	Agency outcome	Preferred term
PBAC	Recommendation	Recommendation
	Rejection	Rejection
	Deferral	Deferral
NICE	Recommended	Recommendation
	Not recommended	Rejection
pCERC	Recommended	Recommendation
	Not recommended	Rejection
IQWiG	Major additional benefit	Recommendation
	Significant additional benefit	Recommendation
	Marginal additional benefit	Recommendation
	No quantifiable additional benefit	Recommendation
	No additional benefit	Recommendation
	Less benefit	Rejection
TC	ASMR = I	Recommendation
	ASMR = II	Recommendation
	ASMR = III	Recommendation
	ASMR = IV	Recommendation
	ASMR = V	Recommendation
	ASMR = VI (SMR = Insufficient)	Rejection