CORRESPONDENCE

Registration and Reimbursement of New Cancer Medicines in Australia

I read with interest the article by Macaulay et al. [1] in a recent issue of *Value in Health Regional Issues* for Asia on the registration and reimbursement of certain medicines for patients with cancer in Australia. This topic is of considerable public interest in Australia given the current Senate inquiry on timely access to new medicines for patients with cancer on the Pharmaceutical Benefits Scheme (PBS) [2]. I have a number of concerns with this study.

First, the objective(s) is not clear. The article states that the objective of their research was “to define the conditions under which [oncologic] drugs lacking phase III supportive data could achieve both TGA regulatory approval and public reimbursement through PBAC approval and PBS listing.” The authors extracted information from European Medicines Agency (EMA) and Food and Drug Administration (FDA) documents, which seems odd given that they have no bearing on Pharmaceutical Benefits Committee (PBAC) considerations. I could understand the inclusion of EMA and FDA information in the study if the authors sought to compare Therapeutic Goods Administration (TGA) outcomes with EMA and/or FDA outcomes, but this was not a stated objective.

Second, the study period is not clear. Public Summary Documents have been published by the PBAC since mid-2005, and Australian Public Assessment Reports (AusPARs) have been published by the TGA since 2010. Insofar as “all publicly available TGA AusPARs and PBAC Public Summary Documents up to October 1, 2014 were screened to determine on what level of supportive clinical trial evidence was based,” this suggests a study period from 2010 to October 2014. Figure 1 suggests a study period from 2004 to 2014. AusPARs are available for just 2 of the 10 medicine/indication pairings in Figure 1. The authors have assumed that the clinical data used to support the PBS listing of the remaining eight medicine/indication pairings in Figure 1 was the same data set that was used to support their registration by the TGA (and elsewhere). This issue has not been discussed.

Third, the authors have not defined or discussed some key concepts. The footnotes to Table 1 state that some medicines were granted “restricted approval” by the TGA and the EMA. This term is not used by the TGA; therefore, it is unclear what they mean. The authors make frequent reference to the “PBAC reimbursement approval” process. The PBAC does not “approve” the reimbursement of new medicines; that responsibility lies with the minister, the cabinet, or both.

Fourth, their study contains a number of errors. The statement that “six of the eight PBAC-approved indications included economic modeling as a cost-benefit approach” is incorrect; none was recommended on the basis of a cost-benefit analysis. The economic evaluation in the submission to support the listing of imatinib mesylate for use by patients with aggressive systemic mastocytosis (ASM), dermatofibrosarcoma protuberans (DFSP), hypereosinophilic syndrome - chronic eosinophilic leukemia (HES-CEL), and MSD/MPD did not include a modeled evaluation [3]. Figure 1 states that the PBAC appraised cetuximab for metastatic colorectal cancer in 2004. The PBS listing of cetuximab for metastatic colorectal cancer involved eight submissions (seven rejections and one recommendation) over a 5-year period; the first submission was considered by the PBAC in March 2005. The clinical evidence in the eight submissions was not the same [4]. Their data set does not include arsenic trioxide for the treatment of patients with acute promyelocytic leukemia, which was recommended by the PBAC in March 2009 on the basis of 11 open-label, single-arm studies [5]. The omission of this medicine from the data set is odd given that it was included in the data set of a similar study conducted by O’Leary et al. [6] that was presented alongside the authors’ poster at the recent International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Asia-Pacific Conference in Beijing [7].

Fifth, the conclusion includes an extensive discussion on issues such as the registration and reimbursement of new medicines for patients with melanoma in Australia and elsewhere, the reimbursement of crizotinib in Australia and elsewhere, codependent technologies, and the need for a fast track regulatory process in Australia, which are not directly related to the stated objective of the study. The Australian reimbursement submissions for ipilimumab, dabrafenib mesylate and vemurafenib (melanoma), and crizotinib (non–small-cell lung cancer) were all supported by phase III clinical data [8–11]. Crizotinib has since been recommended by the PBAC and listed on the PBS [12].

Reference is also made to the rapid FDA approval of pembrolizumab for certain patients with melanoma based on phase I clinical trial data. The PBAC recommended the PBS listing of pembrolizumab at its scheduled meeting in March 2015 with randomized phase III clinical trial data; on June 28, 2015, the Minister of Health announced that it would be listed on the PBS on September 1, 2015 [13]. The PBAC considered a submission to list nivolumab for certain patients with melanoma at its scheduled meeting in early July 2015 [14].

The authors have formed the view that the TGA review process is slow, and they “recommend that Australia explore the ideas of Europe and the United States in expedited access programs and adaptive licensing to ensure that Australian patients with life-threatening diseases with no efficacious treatment options can receive timely access to promising therapies.” They present no empirical data to support such a recommendation. A later registration date in Australia does not indicate that the TGA review...
process is too long by international standards. One needs TGA submission dates to evaluate this hypothesis, but they are not in the public domain. Recent experience with some high-profile oncology medicines does not support their recommendation; pembrolizumab was registered and “approved” for reimbursement in Australia before it had been registered let alone reimbursed in Europe. Dabrafenib mesylate was registered by the TGA on August 27, 2013, and listed on the PBS, with a codependent technology, on December 1, 2013; it was registered in Europe on August 26, 2013, and “recommended” by the Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Healthcare), Transparency Commission (TC), and the National Institute for Health and Care Excellence in December 2013, May 2014, and October 2014, respectively. A specifically designed study is required to examine this issue properly.

Finally, the authors’ finding that data packages lacking phase III pivotal trial data can support regulatory approval and reimbursement for oncologics in Australia is not new. It is well known in Australia that the TGA is prepared to register and the PBAC is prepared to recommend the listing of a new oncology medicine with no supporting phase III clinical trial data. The rapid registration and reimbursement (PBS listing) of imatinib mesylate in 2001 for certain patients with chronic myeloid leukemia is a prime example [15]. The PBAC has recommended the PBS listing of new medicines in multiple therapeutic areas even though it considered the supporting clinical data to be of poor quality [16]. The authors have not examined whether data packages that lack phase III pivotal trial data can support the registration and reimbursement because they will be used to treat patients with a life-threatening disease (e.g., cancer) or because they will be used to treat patients with a rare disease/condition (e.g., orphan drug). Nine of the 10 medicine/indications in their data set have been designated as orphan drugs/indications by the TGA. There are other instances in which the TGA has registered and the PBAC has recommended the PBS listing of a new orphan drug for use by patients with diseases other than cancer on the basis of phase II clinical trial data [17,18]. A recent study compared the likelihood and timeliness of reimbursement for orphan medicines with nonorphan medicines in Australia between 2005 and 2012 [19].

In conclusion, the findings from the study by Macaulay et al. [1] provide no new insights to the current debate in Australia on the timely subsidized access to new cancer medicines. Their recommendations are unsubstantiated.

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REFERENCES


