Access to Cancer Medicines report

Submission by Amgen Australia to Medicines Australia Oncology Industry Taskforce

October 2013

Executive Summary:

Amgen welcomes the publication of the Deloitte Access Economics report outlining the barriers to access to oncology medicines in Australia.

We hope that the report will be the catalyst for a broader community dialogue on the issues affecting cancer treatments. In this regard, Amgen would like to see active stakeholder discussion through broad-based forums in order to develop system improvements for the benefit of cancer patients.

Cancer medicines face particular challenges which will require innovative approaches if timely subsidised access to the latest treatments are to be a reality for patients.

The system of Health Technology Assessment, which underpins the process of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC), needs to evolve to take account of various benefits which are particularly important in the cancer setting.

Consumers also need to be more prominent in deciding what the system of universal access should fund and in assisting the decision makers on individual cancer medicines.

INTRODUCTION

About Amgen:

A biotechnology pioneer since 1980, Amgen Inc. (Amgen) has grown to be the world's largest independent biotechnology company. For nearly 30 years, Amgen has been at the forefront of modern biotechnology by inventing and pioneering industry-leading technologies.

Amgen's medicines treat serious illnesses. We have a presence in more than 50 countries worldwide and have reached millions of people in the fight against cancer, kidney disease, rheumatoid arthritis, bone disease and other serious illnesses. Our medicines typically address diseases for which the number of effective treatment options is limited, or they are medicines that provide a viable option to what is otherwise available.

A significant proportion of Amgen's pipeline comprises innovative oncology medicines.

Amgen Australia Pty Ltd (Amgen Australia), a subsidiary of Amgen, was established in 1991, although Amgen's clinical research in the region actually started much earlier. In 1987 early development work in the area of supportive treatment for cancer patients was carried out at The Royal Melbourne Hospital. Since these early days Amgen has had a rich history of conducting clinical research in Australia. Amgen Australia employs around 150 people, markets 8 products and generates revenue of around A$228.5 million per annum in Australia.

Amgen Australia invests around A$30-35 million in local research and development annually, which represents around 15% of its annual sales. Amgen Australia's clinical research activity in Australia:

- contributes disproportionately to Amgen's global clinical trial effort by consistently being in the top 5 countries for active clinical studies.
- consistently contributes 7-10% of patients to the Amgen global pool of studies in which the subsidiary participates.
- involves on average two First in Human (FIH) studies every year.

Amgen Australia is one of the companies involved in the Medicines Australia Oncology Industry Taskforce because we want to ensure there is broader community dialogue on the issues affecting cancer treatments, and system improvements for the benefit of future cancer patients.

This submission will consider:

1. the costs of developing cancer medicines
2. the particular challenges faced by cancer medicines in relation to subsidised access
3. the need for the system of Health Technology Assessment to evolve to take account of various benefits which are particularly important in the field of cancer
4. the approach taken in other countries
5. the need for the consumer voice to be more prominent in decision making

1. The costs of developing cancer medicines

Today's biologic medicines have made a significant difference to the lives of patients with serious illnesses, including cancer, blood conditions, auto-immune disorders such as rheumatoid arthritis (RA) and psoriasis, and neurological disorders like multiple sclerosis.

According to PhrMA[1], there are more than 3000 projects in development for cancer medicines of which 80% are first in class i.e. a medicine that uses a different mechanism of action from any other already approved medicine.

Such medicines offer new treatment options for patients, particularly for those who have not responded to existing therapies or where no existing treatment option exists.

The large proportion of first in class medicines reflects scientists' rapidly growing knowledge about the molecular underpinning of these diseases and their diversity. For example, 100 years ago leukaemia and lymphoma were considered to be one disease but today the two are known to encompass about 100 individual diseases.

A study by DiMasi and Grabowski[2] noted that new oncology medicines tend to be distinctly different in terms of regulatory status and development metrics. They noted that:

- a substantial majority (70%) of first approvals for marketing of oncology drugs received priority reviews from the FDA compared with other new medicines (40%)
- however clinical development times were longer on average for oncology medicines; and
- the R&D cost per approved new drug for development was 20% higher for oncology drugs compared to the average for all drugs

Small patient populations contribute to the high cost of cancer medicines

The cost of cancer medicines is high compared with medicines which treat broad populations, because cancer is not one disease, but many diseases often involving small sub-populations within one broad cancer type. Development costs are relatively high for these treatments because trials in small populations must be run in many sites and over long periods of time in order to recruit sufficient patients, who are often difficult to identify. Patient identification itself may require costly and elaborate testing. High development costs and small populations in turn influence the price sought by companies to recoup the cost of investment.

A handful of cancers (breast, prostate, bowel, lung and melanoma) are relatively common however, the majority of cancers represent small populations. Excluding the common cancers, all other cancer types each have an incidence of less than 25 per 100,000 population.[3]

As highlighted in the Deloitte Access Economics report, many of the cancer medicines currently in clinical development are for small population cancers and this also is true of Amgen's pipeline. Most of the cancer medicines Amgen has in phase II/III trials are for small population cancers including ovarian cancer (trebananib), gastric cancer (rilotumumab), acute lymphoblastic leukaemia (blinatumomab) and non-Hodgkin's lymphoma (blinatumomab).[4] Small population cancers are often where clinical need for effective new treatments are highest.

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[1] PhrMA. The Biopharmaceutical Pipeline:Evolving Science, Hope for Patients. January 2013

[2] J.A. DiMasi and H.G. Grabowski. Economics of new oncology drug development. Journal of Clinical Oncology, 25(2) January 2007

[3] Deloitte report Chart 2.8

[4] http://wwwext.amgen.com/science/pipe.html

The identification of an appropriate biomarker can enable treatment to be limited to patients most likely to benefit, resulting in these small patient populations being even more narrowly defined. This is an increasingly common feature of cancer treatments in development.

An example from Amgen's pipeline is rilotumumab which is in development for gastric cancer. Rilotumumab is a fully human monoclonal antibody designed to inhibit a particular molecular pathway, called the hepatocyte growth factor/scatter factor (HGF/SF): MET pathway, which has an important role in gastric tumour progression and metastatic spread. In an exploratory analysis, the addition of rilotumumab to chemotherapy in patients with gastric tumours with high MET expression improved median overall survival (OS) from 5.7 months to 11.1 months (HR = 0.29, 95 percent CI, 0.11 - 0.76). Conversely, in patients with gastric tumours with low MET expression, the addition of rilotumumab to chemotherapy was associated with a trend towards unfavourable OS (HR = 1.84, 95 percent CI, 0.78 - 4.34).[5]

These results have led Amgen to plan a Phase 3 study to confirm the efficacy of rilotumumab in the subset of advanced gastric cancer patients selected based on the 'high MET expression' biomarker. It is worth noting that high MET expressors constitute less than 10% of gastric cancer patients.[6]

Cost of manufacturing biologics contribute to high cost of cancer medicines

Many of the innovative medicines being developed to treat cancer are biologic medicines.

The manufacture of biologics is a highly demanding process. Protein-based therapies have structures that are far larger, more complex, and more variable than the structure of drugs based on chemical compounds. Plus, protein-based drugs are made using intricate living systems that require very precise conditions in order to ensure product consistency. The manufacturing process is, therefore, very complex and consists of four main steps:

1. Producing the master cell line containing the gene that makes the desired protein
2. Growing large numbers of cells that produce the protein
3. Isolating and purifying the protein
4. Preparing the biologic for use by patients

The science of manufacturing biological medicines requires expert staff, advanced science and specialized technology.

2. Cancer medicines face particular challenges that will require innovative approaches if timely subsidised access to the latest treatments are to be a reality for patients:

True value of oncology medicines is not available when first approved

Cancer is a complex, life-threatening cluster of diseases and the clinical development process for oncology therapeutics is equally and understandably complex. When any new drug or biologic reaches the requisite regulatory agency (e.g. FDA/TGA) review, it has already undergone years of research in the lab, in animal models, and in patients. Due to the complicated nature of cancer, clinical research for these medicines takes an average of 1.5 years longer than treatments for other disease areas.[7]

[5] Amgen press release. http://www.oncuview.tv/portals/0/linkedfiles/Rilotumumab%20(AMG%20102)%20ASCO_05-16-12.pdf
[6] Lennerz, Journal of Clinical Oncology, 2011, 29 , 4803-10; Graziano, Journal of Clinical Oncology, 2011, 29, 4789-95.
[7] DiMasi, JA and Grabowski HG. Economics of New Oncology Drug Development. Journal of Clinical Oncology, 2007, 25 (2), 209-216

Even with this extensive testing, the clinical benefit demonstrated by the data at the time of initial regulatory approval is often constrained because of the nature of oncology clinical research. Because of ethical concerns and regulatory requirements, pre-approval research is generally focused on proving safety and efficacy for the proposed indication(s), rather than on demonstrating the full intrinsic therapeutic value of the treatment.[8]

Due to the life-threatening nature of cancer, ethical standards are at the forefront of caring for patients and play a significant role in shaping cancer research and treatment. An oncologist must rely on proven therapies with known risks and benefits when treating newly diagnosed cancer patients.[9]

Only after the therapy has demonstrated efficacy in patients with late-stage disease or disease that is resistant to standard therapy can it be tested in earlier-stage cancers or as a first-line therapy. It is typically at these earlier stages that a new treatment is more likely to significantly improve patient survival by modifying the course of the disease by slowing or halting its progression.[10]

As a result, investigational therapies are typically tested first in patients with advanced-stage cancer who have exhausted existing standard treatment options. These late-stage patients typically have been heavily pre-treated and have already failed most available treatments. While this does not impact the actual intrinsic properties of a therapy, it creates a theoretical "ceiling" on the amount of clinical benefit that can be observed during the initial phases of research.[11]

Issues associated with evidence generation: Endpoints

The Deloitte Access Economics report notes that overall survival (OS) is often considered as the most clinically relevant and meaningful endpoint in oncology, especially for medicines that treat advanced-stage cancer. Whilst the TGA often accepts other endpoints, such as progression free survival (PFS), as a basis for registration, the PBAC has a stated preference for demonstration of OS over other endpoints in the cancer setting.

As discussed in the Deloitte Access Economics report, an analysis of OS can be challenging in the cancer setting because it requires larger patient numbers and longer follow-up than other endpoints.

The longer timeframe increases the potential for confounding factors to be introduced such as differences in patient characteristics and subsequent management following discontinuation of trial medication.

The longer timeframes are also inherently problematic for diseases with relatively short survival, so there needs to be a balance between the preference for perfect evidence in an imperfect setting.

While the PBAC has developed a framework for the use of surrogate endpoints, it may not be translating into timely access to cancer medicines, as hoped for. There needs to be a greater discussion around these issues in the cancer setting.

[8] Boston Healthcare. Recognising Value in Oncology Innovation, White Paper, June 2012, 7
[9] Ibid,7
[10] Ibid,7
[11] Ibid, 7

Issues associated with evidence generation: Crossover

Another major source of confounding of OS analysis arises when, for ethical reasons, cross-over from the control arm to active therapy is allowed on disease progression. Some Ethics Committees expect a trial to offer patients the chance to cross-over to the other treatment arm, for that Committee to consider the study to be ethical and approve it. Amgen is able to provide the below example of where confounding due to cross-over has been problematic for one of its cancer therapeutics.

Amgen manufacturers a medicine called panitumumab (Vectibix®) used in the treatment of metastatic colorectal cancer. Panitumumab is very similar to another medicine, cetuximab (Erbitux®), as they are monoclonal antibodies from the same epidermal growth factor receptor (EGFR) inhibitor class.

The efficacy of these treatments in the 3rd-line metastatic colorectal cancer setting, compared with best supportive care (BSC), was assessed in separate but very similarly designed clinical trials, one key difference being that cross-over from BSC to active therapy on disease progression was permitted in the panitumumab trial but not in the cetuximab trial.[12]

In the Amgen trial of panitumumab, 76% of patients who were receiving BSC (i.e no active therapy) crossed over to active therapy. In the cetuximab trial, only 17% of patients "effectively crossed over".[13] The cetuximab trial demonstrated a statistically significant difference in OS (HR: hazard ratio, 0.55; 95% CI, 0.41 to 0.74; P<0.001).[14] The panitumumab OS results were confounded by the high level of cross-over and the difference in OS was not statistically significant (HR, 0.99; 95% CI, 0.75 to 1.29).[15]

In the same trials, the two treatments performed similarly in terms of outcomes not influenced by cross-over including PFS and objective response rate. Panitumumab and cetuximab have been considered similarly effective treatments by the medical community, despite the non-significant OS outcome for panitumumab, and the peak clinical guidelines recommend a choice of either agent in the later-line setting.[16]

As an increasing number of active new drugs are approved, it may become unrealistic to use OS as a meaningful endpoint. Indeed, the benefit of new drugs on OS will be smaller when these drugs are compared with alternative treatments than when they are compared with BSC alone, particularly because patients tend to move from one active treatment to the next active treatment, diluting the impact of each individual active treatment on OS.

The alternative would be not to allow cross-over to the other treatment arm; nevertheless, this option may be unrealistic, because new and potentially effective drugs should not be denied to patients with advanced cancer. The validity of other endpoints should be discussed and methods to deal with uncertainty considered.

Time to progression, for example, usually requires smaller clinical trials and may be more rapidly assessed than trials using OS as an endpoint. This endpoint also has the advantage

[12] Panitumumab: Van Cutsem E et al. J Clin Oncol 2007;25(13): 1658-1664. Cetuximab: Jonker D et al. N Engl J Med 2007 357(20): 2040-2048.
[13] Five patients assigned to receive supportive care alone subsequently received cetuximab off protocol. Ibid, Jonker, 2043
[14] Result for KRAS wild-type population presented. From Karapetis C et al. N Engl J Med 2008;359:1757-65.
[15] Results for KRAS wild-type population presented. From Amado R et al. J Clin Oncol 2008; 26(10): 1626-1634.
[16] Schmoll et al. ESMO Concensus Guidelines for management of patients with colon and rectal cancer. A personalised approach to clinical decision making. Annals of Oncology 2012;23:2479-2516. National Comprehensive Cancer Network Inc 2012. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. Version 3.2012 .

of not being confounded by subsequent therapies. There are also statistical methods designed to adjust for potential confounders affecting the likelihood of crossover and/or survival which have and should continue to be considered and discussed. This issue has been recognised by the PBAC in the past and resulted in the PBAC asking its Economics Sub-Committee to review various modelling techniques for dealing with early cross-over. Industry has yet to be informed of the outcomes from ESC's consideration.

Issues associated with low priced comparators

New medicines are introduced less frequently for low incidence diseases. As such, there may be instances where the comparator for a new treatment is an older, low priced generic medicine.

It may be difficult to show favourable cost effectiveness for such a product, working on the assumption that incremental cost effectiveness ratios (ICERs) of $50K or less per quality adjusted life year (QALY) are usually favoured by the PBAC.

This is illustrated by the grid outlined in Table 1 that summarises ICER values for a hypothetical new high cost drug based on varying comparator prices, under QALY gained assumptions typical of the incremental benefits seen in the advanced cancer setting.

The comparison of a new medicine with a price of $30,000 with a comparator with a price of $20,000 would represent the situation of a high cost targeted therapy versus a somewhat less expensive targeted therapy. The $30,000 versus $5,000 comparator price represents the situation whereby the new targeted therapy is compared to a low priced off-patent medicine.

The grid indicates that when a high cost medicine is compared to a low priced off patent medicine, it is generally not possible to obtain an acceptable ICER. As noted in the Deloitte Access Economics report, the practice of setting reimbursed prices for new medicines with reference to older comparators may sometimes be an obstacle to patient access to innovative cancer medicines.

Table 1: Cost-effectiveness grid

New Drug cost	Comparator cost	Cost per QALY gained	
		0.5 QALY	0.25 QALY
$30,000	$20,000	$20,000	$40,000
$30,000	$10,000	$40,000	$80,000
$30,000	$5,000	$50,000	$100,000

QALY gains of around 0.25 (e.g. from 4 months additional survival at less than full health) are typical of the incremental gains seen in the cancer setting. If there is a large differential in price between the new drug and comparator, a much greater incremental benefit would be required for the cost effectiveness ratio to be in the acceptable range. As shown in the cost effectiveness grid above for the $30,000 vs $5,000 scenario, the QALY gain would need to be at least twice what is typical in the cancer setting, e.g. 8 months compared with 4 months.

Issues associated with valuing incremental improvements

As PhRMA has noted[17], progress does not happen with one breakthrough but rather incremental stepping stones. Each new cancer medicine whether it extends a life by 6 months or 3 years, reflects the cumulative nature of medical discovery.

In addition, as each new medicine is used in the real world – earlier in the disease stage and in combination with other medicines - its full value is realised. This step by step transformation has led to increased survival, improved patient outcomes and enhanced quality of life for many cancer patients. PhRMA has identified a range of impressive gains in survivorship for cancer patients:

- Between 1988 and 2000, improvements in cancer survival created 23 million additional life years
- Treatment advances for Chronic Myeloid Leukemia (CML) have increased the 10 year survival rate for CML patients from less than 20% to more than 80%
- Childhood cancer survival rate is 80% today, compared to 50% in 1970

Breast and colon cancers are examples of where a series of relatively modest gains have resulted in significant improvements over a 10 year period. For example, in breast cancer, there has been evolution in chemotherapy regimes, hormone treatments, biomarkers and bone modifying treatments, all of which are leading to success in beating this cancer.

For cancer medicines particularly, it is important the health technology assessment (HTA) processes accept and recognise the limitations on data at "launch" and do not deny reimbursement too readily. It is only by patients being able to access each new development and doctors being able to gain experience that step-wise progress is made.[18]

Co-dependent technologies

As noted in the Deloitte Access Economics report, some targeted cancer medicines have the advantage of being associated with known biomarkers which, through testing of tissue or blood samples, enable use of therapy in a subset of patients most likely to respond.

This has clear advantages for patients and payers but the requirement for assessment through the co-dependent pathway adds significant complexity and time to the Australian reimbursement process.

A review by Amgen of applications posted on the Medical Services Advisory Committee (MSAC) website confirmed that the requirement for co-dependent technology assessment by PBAC and MSAC is more common in cancer than any other disease: 10 of the 11 current or recently completed assessments which involved the combination of a drug treatment and a response biomarker were for cancer medicines.[19]

Drugs like Amgen's rilotumumab will have a more uncertain evaluation pathway and take substantially longer to become available if reimbursement of an associated diagnostic test is required, under the current paradigm. It is timely to review the system to ensure it keeps pace with rapid changes in testing methods and biomarker development.

[17] PhRMA Cancer Medicines are worth it. April 25, 2013
[18] PhRMA. Value of Innovative treatments for Cancer. April 2, 2013
[19] http://www.msac.gov.au/internet/msac/publishing.nsf/Content/home-1

3. The system of Health Technology Assessment which underpins the process of consideration by the PBAC process needs to evolve to take account of various benefits which are particularly important in the field of cancer.

Health benefits in the Australian reimbursement system are typically measured in terms of number of quality-adjusted life years (QALYs) gained. The QALY is a combination of the value of the health states and their duration, and every QALY is equivalent to one year of life in full health.

It is the de facto standard in cost utility analysis that the sole objective of healthcare is to maximise the number of QALYs gained, irrespective of to whom those QALYs go and how they are distributed across society. There is evidence to suggest that people attach a premium to severity of illness.[20] It could be that treatments for patients with advanced cancer have greater personal and social value than do treatments producing equal QALYs in other settings.

A research paper by the Office of Health Economics[21] (OHE) found that the methods currently being used to assess health benefits when evaluating healthcare technologies for cancer and other end of life diseases have real limitations in terms of their ability to accurately capture the value of the health gains deemed important by cancer patients.

The objective of the Office of Health Economics paper was to examine how well the QALY captures the health gains generated by cancer treatments, with particular focus on the methods for constructing QALYs preferred by the National Institute for Health and Care Excellence (NICE). It is recognised that the PBAC does not have a fixed QALY threshold like NICE, however, the research paper identifies issues which could have some relevance to PBAC evaluation.

Three key issues emerge. First, the EQ-5D, NICE's preferred measure of health-related quality of life in adults has been found to be relatively insensitive to changes in health status of cancer patients. The PBAC has an expressed preference for utilities derived from a multi-attribute utility index (MAUI), such as the EQ-5D, in a direct randomized controlled trial. It is, however, acknowledged in the PBAC guidelines that a limitation of MAUIs is their potential insensitivity to some patient-relevant outcomes.[22] Second, the time trade-off, NICE's preferred technique for estimating the values of health states, involves making assumptions that are likely to be violated in end-of-life scenarios.

Third, the practice of using valuations of members of the general population, as recommended by NICE, is problematic because such individuals typically display a misunderstanding of what it is really like for patients to live with cancer. A growing body of empirical evidence indicates that patients tend to value a given health state more highly than non-patients. The paper suggests that until there are improved evaluation processes in place, bodies such as NICE need to explicitly recognise the limitations of the QALY when assessing cancer treatments. In cases where the QALY is likely to undervalue the actual health benefit accruing to cancer patients, a deliberative decision making process should be adopted where the implications of adopting alternative methods for constructing QALYS are considered alongside the clinical and cost effectiveness evidence.

[20] Shah K et al. Severity of illness and priority setting in healthcare: a review of the literature. Health Policy 2009;93:77-84.
[21] Garau, M et al. "Using QALYs in Cancer: A review of the methodological limitations" OHE Research Paper 10/01, Oct 26, 2010
[22] Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee, Version 4.3, December 2008.

Amgen believes that any reframing of the HTA system should be underpinned by a set of principles agreed upon through broad stakeholder consultation, so that they reflect societal values.

4. Other countries and collaborations have recognised the need to put in place special arrangements for cancer medicines

The challenges faced in Australia are similar to the challenges faced by other countries where it has been recognised that their usual systems will not effectively deliver for cancer medicines and patients.

In the UK for example, the Cost per QALYs measure utilised by NICE was not delivering access to cancer medicines in line with community or political expectations. They have therefore put in place specific mechanisms to facilitate access to cancer medicines because cancer patients do not have the luxury of time, while the search for a perfect system continues.

UK Cancer Drugs Fund

The Cancer Drugs Fund (CDF) was set up in 2011 to help patients in England access certain drugs before they get approval for widespread NHS use. The scheme was due to end next year, but British Prime Minister David Cameron has recently [23] pledged £400m to keep it running.

There are around 30 drugs that are available on the CDF, and over the last three years about 34,000 patients have received treatment that they would not have otherwise had, had the fund not existed.

The aim of the CDF was to make it easier for doctors to prescribe treatments even if they have not yet been approved by the National Institute for Health and Care Excellence (NICE).

Health Secretary Jeremy Hunt said the government had made an exception for cancer because they considered it "the number one killer", and they thought that “we had a particular problem with a lack of access to these drugs."

The existence of the CDF is indicative of the challenge in ensuring that current UK health technology assessment (HTA) methods and processes are able to work effectively for cancer and other specialist medicines.

The Canadian system

Canada’s public drug plans outside of Quebec have relied upon a national health technology assessment process for oncology medications since 2007. The interim Joint Oncology Drug Review (iJODR) program, established in March 2007, drew upon the expertise of provincial drug plans, cancer agencies, practicing oncology clinicians, tumour-specific oncologists, patients, and innovative pharmaceutical companies. As an interim process, it evolved over time and involved extensive consultations with all affected stakeholders. The result of those discussions was the creation of the pan-Canadian Oncology Drug Review (pCODR) in 2010. Following an 18-month period of organisational evolution, development and extensive consultations, the pCODR review process was launched in mid-2011.

[23] Announcement was in Sept 2013

pCODR was created as a mechanism to provide public funding decision-makers with a rigorous, science-based and independent health technology assessment of new cancer medications in order to assist them in making valid choices about what to fund in what circumstances. It was created to be separate from the existing national HTA review process, the Common Drug Review (CDR), which had been evaluating medicines for participating public drug plans since 2003.

pCODR was created in recognition of certain unique characteristics associated with the manner in which cancer care was managed within the Canadian pharmaceutical marketplace. Among the reasons for the creation of pCODR was the recognition that cancer care is highly specialised and requires diverse expertise. The number of different cancers and the nuances involved in each particular tumour site require access to a range of specific experts and efficient processes to ensure that the right advice is being sought in each case.

The pCODR leadership developed a series of eight principles as a philosophical platform upon which the review process was built and which the organisation follows in its daily work. These principles were broadly reflective of the principles proposed by stakeholders. The eight principles are as follows:

1. Governance - A review process with governance structures that are fair, objective, transparent and accountable to patients, payers and the public
2. Representation – A review process that is multidisciplinary, cross-jurisdictional and collaborative in nature with appropriate representation from diverse stakeholders and linked to other key national initiatives
3. Efficient and Effective – A review process that is cost-efficient, effective and streamlined (i.e. reduced duplication) to support timely decision-making
4. Evaluation – A review process with capacity for data capture and ongoing evaluation (decision monitoring / performance measurement) to support continuous process improvements. In addition, capacity for health outcomes and economic impact analysis to support decision-making and planning
5. Health System Focus - Medications are evaluated within a review process and decision making framework that are consistent with those used for medicines for other diseases
6. Evidence-based - A review process with capacity for rigorous and consistent evidence-based clinical and pharmacoeconomic reviews to support evidence-based decision-making
7. Excellence - A review process that reflects an ongoing commitment to excellence through incorporation of best practices in a spirit of continuous quality improvement
8. Ethical Framework - A review process that includes an ethical framework which balances the need for timely and quality cancer therapies with broader societal values[1]

There have also been other non-cancer specific approaches to try and address issues of evidence. For example:

The Green Park Collaborative

This collaborative is one attempt to provide better combined regulatory and HTA guidance. This international pilot initiative which began in 2010 aims to explore the scientific feasibility of developing guidance for the life sciences industry on the design of clinical studies to meet the needs of HTA organizations such as PBAC.

The intent is to develop both evidence guidance documents by therapeutic area and general methodological advice applicable across therapeutic areas. Ultimately this guidance would

help reduce uncertainty about the evidentiary preferences of regulatory and HTA bodies, improve relevance of clinical research and increase patients access to useful innovations.

5. Consumers need to be more prominent in deciding what the system of universal access should fund and in assisting the decision makers on individual cancer medicines

To ensure that decisions are consistent with and continue to reflect societal values and priorities, a broad range of stakeholders - particularly consumers - should be able to contribute to HTA-based decision-making processes - at the system and individual product level.

While the Australian system provides for consumer representation on the PBAC, and allows for consumer input in relation to individual products, the opportunity for the consumer voice is limited.

Consumers should be able to put forward the evidence that they believe best represents their interest's at all relevant stages of the HTA/HTA-based process and be kept informed about progress throughout the various steps of the HTA (evaluation, appraisal and decision-making). For example, pCODR in Canada uses a deliberative framework to reflect patient input in recommendations.

During the development of the pCODR process, patient groups clearly indicated that they not only wanted the opportunity to contribute to the reviews, but also to be assured that their input would have an impact on recommendations. The deliberative framework which pCODR created to direct its recommendation-making includes patient input as a central component of its four equal considerations. In addition, an assessment of the patient input received is outlined explicitly within the written recommendations, thereby providing stakeholders with assurances that their input was considered.

Where appropriate, consumers should also be represented on relevant advisory bodies and/or committees in terms of system issues.

Conclusion

This submission has aimed to identify the issues which are commonly encountered in the cancer setting and which make it difficult for cancer medicines to demonstrate the clinical benefits that are called for in the current HTA system.

While a perfect solution to this dilemma is not obvious, clearly there is an urgent need for dialogue and debate, to move forward on these issues. Amgen would like to see active stakeholder discussion through broad-based forums in order to develop system improvements for the benefit of cancer patients.

Many cancer patients do not have the benefit of time. To do nothing – to continue to treat access to cancer medicines like all other medicines – will fail patients.