

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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Regulation of Drug Pricing in Australia, England, and New Zealand

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H&O What are the main functions of the National Institute for Health and Clinical Excellence (NICE) in England, the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, and the Pharmaceutical Management Agency (PHARMAC) in New Zealand? How do they differ?

JR Due to the rising cost of pharmaceuticals, many countries instituted agencies to manage government expenditure and drug coverage. Of the 3 countries, Australia has the oldest established agency, started in 1987, followed by New Zealand in 1993, and England in 1999. PBAC and PHARMAC are similar in that they decide what drugs will enter the public formulary for primary care in Australia and New Zealand, respectively; PBAC and PHARMAC evaluate all new drugs. Whereas PHARMAC and PBAC only appraise drugs, NICE appraises technologies (ie, medical devices) as well. NICE also differs from PHARMAC and PBAC in that it does not control access to the formulary for drugs in England. It only evaluates a selection of drugs—approximately 20 per year—referred to it by the government. Because NICE only assesses a selection of technologies per year, the government tries to refer technologies of interest. Another difference is that NICE has several roles other than drug appraisal; NICE is in charge of creating and standardizing guidelines, and covers a much wider range of interventions.

A further distinction between NICE, PHARMAC, and PBAC is in the sale of pharmaceuticals. In Australia and New Zealand, a drug must go through PBAC or PHARMAC in order to be sold to the public sector. In

England, most drugs sold to the National Health Service (NHS) have not been appraised.

H&O What criteria do England, New Zealand, and Australia use to determine the funding of pharmaceuticals?

JR Evaluation criteria vary among the 3 countries. However, they all include clinical and cost-effectiveness and all use cost per quality-adjusted life year (QALY) as an appraisal tool. A key distinction to be made is between assessment and appraisal. NICE deals more with these 2 terms than do PBAC and PHARMAC. Assessment is defined as the science, meaning systematic review and evidence synthesis including cost-effectiveness, and appraisal is the wider term that encompasses other criteria. The other criteria for NICE include the uncertainty of the technology, the nature of the health condition, the innovation of the technology, and wider costs and benefits (Table). Each country has a more or less explicit threshold level for cost-effectiveness (cost per QALY); this threshold is higher in England than in Australia (New Zealand does not have a published threshold). The cost per QALY is determined by estimating the value of a statistical life, generalized from clinical trials. The problem with this method is that a statistical life is an abstract life and may not reflect what happens to actual patients who are denied a drug in a real-life setting.

H&O Are there other factors that drive decision making even if a technology is found to not be cost-effective?

JR In order to maintain a fair and effective evaluation process, NICE consults with the clinical community, particularly with medical societies. NICE has exceeded the threshold of cost per QALY numerous times, and this was

Table. Criteria Used by Regulatory Agencies for Funding New Drugs

England (NICE)	Australia (PBAC)	New Zealand (PHARMAC)
Clinical effectiveness and cost-effectiveness (cost/QALY)	Clinical effectiveness and cost-effectiveness (largely cost/QALY)	Clinical effectiveness and cost-effectiveness (cost/QALY)
Uncertainty	Price of alternative brands or drugs in the same therapeutic class	Health need, including those of Maori and Pacific Islander peoples
Nature of health condition	Budget impact	Budget impact
Innovation of technology	“Rule of rescue” where appropriate	Cost-effectiveness of drugs versus other interventions
Wider costs and benefits		Clinical benefits and risk
Precedents		Direct cost to users
		Availability of alternative treatments

NICE=National Institute for Health and Clinical Excellence; PBAC=Pharmaceutical Benefits Advisory Committee; PHARMAC=Pharmaceutical Management Agency; QALY=quality adjusted life year.

Adapted from Raftery J. *MJA*. 2008;188:26-28.

usually because of the nature of the disease. If a drug has potential to save lives, it is more difficult to reject it solely on the basis of poor cost-effectiveness. The most obvious example of using other factors to drive decision-making is in end-of-life care. NICE states that if patients have less than 2 years to live and the proposed drug offers proof of a substantial increase in life expectancy, then it should be treated differently from other drugs. Other criteria are a small patient population and no comparable treatment on the market for that condition—there is a push for drug approval in the case of indications that do not have any approved therapies. Overall, all 3 countries (England, Australia, New Zealand) have in the past found ways to fund a number of drugs that they deemed politically difficult to reject.¹ Decisions on which drugs to fund in the final evaluation depend on political and social acceptability.

H&O What are the advantages and disadvantages of using cost-effectiveness evaluation (cost/QALY) as a drug appraisal tool?

JR The advantage of using cost-effectiveness is that it maximizes the value obtained for the money spent. If the focus of a healthcare system is improving patient health, then cost-effectiveness is ideal—it is rooted in spending money to the maximum effect. If, on the other hand, a healthcare system is focused on other things, it requires consideration of alternative factors.

There are drawbacks with using cost per QALY. One is a less patient-friendly system. When the focus is on outcomes, the patient’s experience with their doctor, for example, becomes less important. The pharmaceutical industry also perceives value for money assess-

ment as a disadvantage because they see it as a form of price control.

A challenge in applying cost per QALY to new oncology drugs has to do with the value of extending life for patients who are often terminally ill. Instead of an abstract statistical life, decision makers may be faced with actual angry patients who are being denied treatment. As a result, governments can find it hard to defend decisions based on cost per QALY when they encounter an expensive drug which has the potential to save lives, even if only for a few months. Whether these drug prices are justified or not is a major factor and it is further complicated by drugs having multiple indications.

H&O What is reference pricing, and is it applicable in the United States?

JR Reference pricing can involve comparison of drug prices in any one country with that being charged elsewhere. Many European countries look at drug prices of neighboring countries to help determine pricing for their market. Reference pricing can also refer to comparisons within classes of drugs. For example, a new statin would be compared to the going rate of statins already on the market. If a company develops an expensive statin, PHARMAC and PBAC would ask if it works better than existing statins. If there is proof that it does, it may be priced higher. If the efficacy is similar, it will be priced at the average or lowest price of that therapeutic group.

Reference pricing has clear implications for pharmaceutical companies. If a company is aware that their newly developed drug will be compared to other similar drugs, it will assess its competition and strive to obtain a

premium price compared to that of an existing treatment. Premium pricing will result from demonstrating that the drug is superior. Therefore, the questions to ask become “how much better?” and “how much is that improvement worth?”

Seen from the outside, the United States is extraordinary for many reasons. First, given its size, it accounts for approximately half of the global pharmaceutical sales. Second, it has the fewest controls on pricing. It is the most market-oriented country in terms of its drug pricing, and it is also one of the richest countries. The United States is an outlier. What this means is that pharmaceutical companies can sell drugs in the United States at prices higher than those affordable to other countries. Until the United States begins to resolve this problem, healthcare costs will continue to rise for both the United States and the rest of the world.

There is no doubt that reference pricing will be applicable in the United States; it is only a matter of when. The progress is surprisingly slow as is evident by the difficulty that HMO's and insurance companies are facing in trying to control healthcare spending. The high cost of healthcare is one reason many Americans do not have health insurance.

H&O What price regulation reforms would benefit these countries in the future?

JR Rather than price regulation, a better term is value-based pricing because it translates to value for money and can give pharmaceutical companies the appropri-

ate incentives to invest in drugs in the future. It is not only about keeping prices down. Given the current economic prospects, value-based pricing seems a wise direction to take.

Besides the difficult issue relating to end-of-life treatments, the application of cost-effectiveness to many new cancer therapies (eg, trastuzumab, imatinib) has to do with poor evidence. This evidence is often based entirely on a single trial, often one that was terminated early. Trials are often quite small in scale, and patients are of a highly selective population. Therefore, data on efficacy, rather than effectiveness, is achieved. Data on optimal therapeutic duration are often limited; therefore, physicians are uncertain about how long patients should stay on a drug or how they should be treated when they come off. The price of the actual drug may be clear, but its overall cost is not.

Most importantly, the drug effect on life expectancy is still left uncertain because trials are often stopped once a statistically significant difference in study endpoints, such as progression-free survival (PFS), is observed. However, translating PFS into life expectancy, let alone life years or QALY, is tricky; estimates of cost-effectiveness often rely on extrapolating curves and not on real-life practice. The evidence challenge for new oncology drugs is particularly difficult because of the limited data on duration. The future of oncology trials should be about better data and longer follow-up.

References

1. Raftery J. Paying for costly pharmaceuticals: regulation of new drugs in Australia, England, and New Zealand. *MJA*. 2008;188:26-28.