PHARMAC’s response on temozolomide and funding costly medicines that prolong life shortly

Dr David Hamilton (http://www.nzma.org.nz/journal/118-1227/1774) accurately describes the clinical benefits of temozolomide and PHARMAC’s consideration of funding; and how this relates to what price to pay to prolong survival in incurable illnesses. We update progress with the funding of temozolomide, and agree there are dilemmas around the funding of high-cost medicines that give definite if limited survival gains.

Temozolomide

We have moved as quickly as possible to assess temozolomide. It is not usual to carry out a clinical review by PTAC and an economic analysis before a drug is registered by Medsafe and the supplier has made an application to PHARMAC; however this is what was done for temozolomide. Details of timelines can be seen in the Appendix to this letter. Our approach with temozolomide recognised the limited life expectancy for patients diagnosed with glioblastoma multiforme, and their particular needs.

Temozolomide is unfortunately a costly treatment, currently in the region of $40,000 to $50,000 per patient per year, and even with only 50 treated new patients per year this would result in an overall annual cost of around $2 million. For that sort of expenditure our analysis must be robust and the expenditure compared with other areas of need.

We consider that there are a number of reasons to support the funding of temozolomide when considered under PHARMAC’s decision criteria.1 We have also had constructive discussions with the supplier and have sent them a proposal for funding, and anticipate a decision early in 2006.

What value does society place on limited survival gains in incurable disease?

Currently, PHARMAC has funding available for medicines such as temozolomide and has a programme of new investments. However, that funding would not cover all the applications for new medicines that we have received, and funding for out-years is uncertain, so choices between medicines need to be made.

There will always be difficult decisions to make when funding pharmaceuticals within a constrained budget, and these decisions are not going to get any easier. This prioritisation will be particularly tested in coming years, as on the horizon are a number of new oncology drugs and other beneficial high-cost medicines.

Spending on cancer drugs funded from the community pharmaceutical budget has grown from just over $1 million three years ago to nearly $12 million in 2004/05. This makes it one of the fastest-growing areas of expenditure, and some new and expensive treatments are also being considered. Although difficult to obtain reliable data on hospital use of cancer pharmaceutical treatments, our best estimate is that
hospitals spent $35 million in the 2004/05 financial year. Growth in cancer treatment has outstripped growth in spending on other treatments.

Newer oncology drugs are often extremely expensive, often in the range (and sometimes greater than) $50,000 per year per patient—temozolomide and trastuzumab (for breast cancer) being good examples. These drugs will mean that we will all need to continue to make decisions about where New Zealand’s priorities lie. At the moment, expensive treatments, which may offer significant benefits to a small number of people, must compete for limited funds with less expensive medicines that treat large numbers and achieve greater putative population health gains\(^2\) for the same total costs. The growing number of costly new treatments makes such decisions both more common and more difficult.

Relevant to these issues, there has been recent debate in the *Journal* whether PHARMAC should lower the discount rate used in its economic analyses (affecting how medicines are prioritised).\(^3\)–\(^5\) Such issues are important to the funding of medicines that give short-term survival gains, as lower discount rates tend to advantage long-term gains at the expense of short-term.

PHARMAC is currently reviewing its decision-making process for high-cost medicines—driven in part by having to turn down treatments for small numbers of people, who then miss out. PHARMAC’s Board should be considering the outcome of the review process next year; prior to that, any proposed changes to our decision making processes would undergo public consultation.

PHARMAC’s prioritisation process tries to allocate scarce resources in a fair and transparent way—consistent from year to year and medicine to medicine.\(^6\) Transparency in the decision-making is important, so that people understand the decision even if they don’t agree with it. While we have a fixed, albeit increasing, pharmaceutical budget, the issue of rationing—making explicit choices to fund and not fund particular medicines—remains something that New Zealand must keep doing.

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Conflict of interest: Scott Metcalfe is externally contracted to work with PHARMAC for public health advice. Steffan Crausaz, Peter Moodie and Wayne McNee declare no conflicts.

References and endnotes:

   Section 2.2 Decision Criteria


9. PTAC reviewed the application from Schering-Plough and advice received from CaTSoP at its November scheduled meeting. PTAC considered both the Stupp et al 2005 and Athanassiou et al 2005 RCTs—both being on the use of temozolomide as adjunctive therapy in combination with radiotherapy in patients with newly diagnosed glioblastoma multiforme, but with their patient populations differing in the extent of disease progression at randomisation (the patients in the study by Stupp et al had a generally higher performance status than those in Athanassiou et al). PTAC considered that the patient population in Athanassiou et al would be more representative of the patients presenting with glioblastoma multiforme in NZ.

PTAC considered that the available evidence demonstrated that some patients obtain a considerable benefit, with an additional 15% of patients surviving at 2 years compared with radiotherapy alone (median survival benefit 2.5-5.7 months). However, PTAC considered the majority of patients would obtain little benefit from treatment with temozolomide, and that it was appropriate to examine targeting of treatment to those patients likely to benefit from treatment with temozolomide. PTAC considered that, from the data provided, patients with higher performance status (Karnofsky score >80, WHO score 0 or 1) obtained significant benefit with temozolomide treatment; tumour resection (rather than biopsy with no resection) was also predictive of a response.

PTAC recommended that temozolomide should be listed on the Pharmaceutical Schedule for the adjuvant treatment of newly diagnosed glioblastoma multiforme in combination with radiotherapy. PTAC recommended that subsidy should be targeted to this patient group possibly by means of a Special Authority. PTAC considered that patients should have a good performance status (Karnofsky score >80 or WHO score 0 or 1) at diagnosis, and preferably a resectable or partially resectable tumour. PTAC gave a high priority to this recommendation.
PTAC considered that CaTSoP should review any criteria. PTAC considered that a low priority should be given to funding under criteria that included a poor performance score (Karnofsky score <80 or WHO score 2). PTAC also recommended that approvals for funding should be restricted to the initial treatment in combination with radiotherapy followed by a maximum of six cycles of temozolomide.

Appendix: Timeline to date

- 2001: Temozolomide first submitted to the Pharmaceutical and Therapeutics Advisory Committee (PTAC), for use in recurrent glioblastomas post-radiotherapy. The evidence for its effectiveness in this setting was not strong, and PTAC and then its cancer treatments subcommittee (CaTSoP) advises PHARMAC that funding should not be made available.

- March-April 2005: Evidence supporting the use of temozolomide in conjunction with radiotherapy is published in major medical journals.

- PHARMAC asks PTAC to consider temozolomide again in light of the new evidence. This is an unusual step, as temozolomide not approved for use in this way by Medsafe, and no funding application by the supplier of temozolomide (Schering-Plough) to PHARMAC.

- 18 August 2005: PTAC considers the new phase III trial evidence on temozolomide. Seeks specialist advice from CaTSoP, deferring any recommendation until temozolomide approved by Medsafe and the supplier applies for funding.

- 1 September 2005: Medsafe approves temozolomide for use in conjunction with radiotherapy.

- 2 September 2005: Cancer treatments sub-committee of PTAC examines the new phase III trial evidence.

- 18 October 2005: PHARMAC receives new funding application for temozolomide from Schering-Plough.

- October-November 2005: PHARMAC conducts rapid economic analysis of temozolomide.

- 17 November 2005: PTAC considers the new application, making a positive recommendation (viz., recommending with high priority the listing of temozolomide for newly diagnosed glioblastoma multiforme used in combination with radiotherapy, targeted to patients with good performance status at diagnosis and preferably a fully/partially resectable tumour).

- November-December 2005: Ongoing negotiations between PHARMAC and the supplier, including sending the supplier a proposal for funding, aiming for agreement in early 2006.