6 July 2012

The Royal Australian & New Zealand College of Psychiatrists

[redacted]
PBS Post-Market
Department of Health and Ageing
MDP 900
GPO Box 9848
CANBERRA ACT 2601

By email to: PBSpostmarket@health.gov.au

Dear [redacted]

Re: PBAC Review of PBS anti-dementia drugs to treat Alzheimer's disease

The Royal Australian and New Zealand College of Psychiatrists (RANZCP) and the RANZCP's Faculty of Psychiatry of Old Age (FPOA) is delighted to provide preliminary feedback on the PBAC Review of PBS anti-dementia drugs to treat Alzheimer's disease. The RANZCP's final submission will be sent on **Wednesday 11 July 2012.**

The RANZCP would like to raise the following issues for consideration:

- The continuation rates of the continuation of therapy beyond six months is comparable to other jurisdictions such as, the United States of America (USA), where Medicare data reveals the mean number of days of therapy for donepezil, rivastigmine and galantamine to be 226, 206 and 216 days respectively.
- The two point improvement in the Mini-Mental State Examination is an inadequate surrogate marker for the demonstration of patients receiving benefit from Alzheimer medicines.
- The RANZCP respectfully requests the PBAC should broaden their Terms of Reference to consider medical management of Behavioural and Psychological Symptoms of Dementia (BPSD).
- The RANZCP does not agree with the use of the Quality Adjusted Life Years as measure against cost-effectiveness of anti-dementia drugs.

If you would like to discuss any of the issues in regard to this letter, or would like any further information, please contact Dr Roderick McKay, via bianca.mathews@ranzcp.org or by phone on (03) 9601 4968.

Yours sincerely

Dr Maria Tomasic
President

Ref: 2503

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The Royal Australian & New Zealand College of Psychiatrists

11 July 2012

[redacted]
PBS Post-Market
Department of Health and Ageing
MDP 900
GPO Box 9848
CANBERRA ACT 2601

By email to: PBSpostmarket@health.gov.au

Dear [redacted]

Re: PBAC Review of PBS anti-dementia drugs to treat Alzheimer's disease

Further to the initial submission dated 6 July 2012, the RANZCP Faculty of Psychiatry of Old Age (FPOA) is delighted to have the opportunity to address the terms of reference of this review.

We note that the proposed Terms of Reference (TOR) are:

> a. Review recent Australian utilisation data on patient initiation and continuation rates to cholinesterase inhibitors and memantine.
>
> b. Review whether the two point improvement in Mini-Mental State Examination continues to be an adequate surrogate for measuring improvement in patients with dementia treated with these medicines; and are there other more reliable measures of patient relevant outcomes?
>
> c. Investigate if there is more recent evidence on the safety and efficacy of these medicines that would inform the PBAC about their cost-effectiveness.
>
> d. Review the current PBS restriction continuation rule and the likely effect it has on cost-effective utilisation of these medicines.

In relation to the proposed TOR, we note the findings of the Drug Utilisation Sub-Committee of the PBAC that were published last year [1]. A key finding of this review was that continuation of therapy beyond six months was higher than expected on the basis of clinical trial response rates. Whilst not disputing that this is the case, we note that the continuation rates in Australia are comparable to those in other jurisdictions, notably the United States of America (USA), where Medicare data reveal the mean number of days of therapy for donepezil, rivastigmine and galantamine to be 226, 206 and 216 days respectively [2].

We submit that the two-point improvement in Mini-Mental State Examination is an inadequate surrogate marker for the demonstration of patients receiving benefit from these medicines. Published analyses have demonstrated that patients receiving cholinesterase inhibitors will have more favourable cognitive outcomes than placebo-treated patients for at least 6 months, after which times their performance begins to converge with those receiving placebo [3]. In other words, patients do not need to *improve* cognitively in order to benefit from these drugs: either the maintenance of an existing level of cognitive performance, or the slowing of ongoing cognitive decline are relevant patient outcomes, and we would urge the PBAC to broaden the TOR to consider patient benefit in terms other than cognitive improvement. This issue is of particular relevance to the criteria that must be met in relation to the continuation of memantine beyond the initial six-month PBS approval period. We note with some concern that, of the pivotal clinical trials that led to the PBS listing of the drug [4, 5] the main efficacy data were in relation to activities of daily living, Clinician's Interview-Based Impression of Change plus caregiver input (CIBIC-Plus).

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We note that there is considerable evidence that cholinesterase inhibitors are effective in the management of behavioural and psychological symptoms of dementia (BPSD) and that the use of these drugs is an appropriate pharmacological strategy in this setting [4]. With the choice of alternative agents used to treat BPSD being constrained by significant safety and tolerability issues, we would ask that the PBAC consider broadening its TOR to consider the additional question of whether the existing PBS indications should be broadened to include BPSD in the setting of severe dementia.

There is evidence that cholinesterase inhibitors can have measureable benefits in cognition, global function and activities of daily living in patients with severe AD [5, 6]. We submit that the current review should consider the question of broadening the PBS indications for the use of these drugs to include their use in patients with severe dementia.

In terms of the cost-effectiveness of the anti-dementia drugs, we note that cost-effectiveness is often measured using the Quality Adjusted Life Years. This methodology has been criticized, rightly in our opinion, as being inherently discriminatory against the aged [7]. We would suggest that the proposed TOR take a broader approach to the measurement of cost-effectiveness of these drugs, and note the evidence that for each additional month of cholinesterase treatment, a reduction of 1% in total all-cause health costs can be demonstrated [2].

We note the increasing body of evidence suggesting that cholinesterase inhibitors have demonstrable benefit in dementias other than Alzheimer's disease [8-10] and would ask that the PBAC consider this evidence as part of the enquiry's TOR.

If you would like to discuss any of the issues in regard to this letter, or would like any further information, please contact Dr Roderick McKay, via bianca.mathews@ranzcp.org or by phone on (03) 9601 4968.

Yours sincerely

Dr Maria Tomasic
President

Dr Roderick McKay
Chair, Faculty Psychiatry of Old Age

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