Review by the Pharmaceutical Benefits Advisory Committee of the subsidy for anti-dementia drugs to treat Alzheimer's Disease
Submission by A/Prof Mark Yates

I apologise for the late submission and fully accept that this submission could be disregarded. I have provided my comments in Blue and attached two documents.

The Terms of Reference for the Review are:

a. Review recent Australian utilisation data on patient initiation and continuation rates to cholinesterase inhibitors and memantine.

Attached to this submission is a spreadsheet documenting 60 patients treated in the Grampians CDAMS clinic from 1996 to 2001. The patients were sourced by a word search of all letters from the clinic that had the words Aricept/ Donepezil, Exelon/Rivastigamine or Reminyl/Galantimine and then reviewing all the patient files identified.

This data set shows that in this clinic of 48 patients who took the recommended medication for at least 3 months 25 (52%) achieved a 2 point improvement on the MMSE. This figure is close to that identified by the published DUSC review. This data should not be put on the website.

More recent data could be collected but as the process in the clinic has not changed I doubt there would be any difference now.

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?

It will be unlikely a more reliable yet readily used surrogate measure will be found. The DUSC data does not demonstrate rampant misuse the growth reflecting the prevalence growth if not a little less.

Two points on the MMSE is well established. The ADAS Cog score improvements of 4 points is a harder to achieve in the population where it is used (MMSE >24) because the ADAS scores in this group are low (16-10) where the change is considerably less than the 4 point annual change seen in the naturalistic studies on which this figure was based.

I have attached some short de-identified patient stories collected in 2000 that add clinical perspective to this change. As Ballarat is a small community this data should not be put on the website.

It is reasonable to to suggest that clinical judgment be the best way to evaluate change and then do away with the complexity of specified outcome measures. This has some merit but some patients and families are desperate for treatment and in my clinical experience to have a measure that is not achieved can be helpful. It is also clear that a large number of people with AD do not get offered Ad symptomatic treatment and this reflects a lack of engagement with the Primary Care. I think there is real value for Primary Care to have access to the AD treatments with appropriate support but in the first instance a well understood outcome measure will be important.

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.

The data here is concerning but changes to outcome measure will not make a difference. Some of the anitcholinergics used are understandable and in the doses used have minimal anticholinergic effect. The use of oxybutinin is of more concern.

d. Review the current PBS restriction continuation rule and the likely effect it has on cost-effective utilisation of these medicines.

I would not recommend any change to the current innitiation guidelines. I suggest the addition of a stopping rule pertain to admission to High Level Residential Care that is necessary because of progression of the dementia. In this situation a trial cessation of the AChI should occur 2-3 months post admission. The AChI should only continue if there is a substantial change in behavioural of motor performance. The reason to delay this trial by 2-3 months is to allow the patient to settle into their new environment before removing a medication the family or staff feel may be helping the patient.

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