The Royal Australasian College of Physicians

PBAC Review of Pharmaceutical Benefits Scheme anti-dementia drugs to treat Alzheimer's disease

Submission by The Royal Australasian College of Physicians

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The Royal Australasian College of Physicians (RACP) welcomes the opportunity to provide a submission to the Pharmaceutical Benefits Advisory Committee (PBAC) Review of Pharmaceutical Benefits Scheme (PBS) anti-dementia drugs to treat Alzheimer's disease.

Executive Summary

It is clear that there remains no medical or pharmacological treatment for Alzheimer's disease or dementia that can reverse or stop the progression of the disease. Anti-dementia drugs, particularly the cholinesterase inhibitors for people with mild to moderate Alzheimer's disease and memantine for people with moderate to severe Alzheimer's disease, are intended for symptom management to help improve cognition, function, behaviour, language and quality of life.

Patients undergoing therapeutic treatment may experience no response; a modest improvement in cognitive function, behaviour and ability to complete activities of daily living; or may not tolerate the treatment due to adverse side effects. The effect experienced by the patient may vary according to the drug prescribed – that is, although the patient may not respond to donepezil, they may experience some symptomatic relief with galantamine.

Despite the modest efficacy of therapeutic treatment, the RACP supports the continuation of anti-dementia drugs on the PBS because, where the treatment is effective, it can improve quality of life for the person with Alzheimer's disease and their carer. This improvement may not be confined to cognition or language skills (as measured by the MMSE) but may also include an improvement in behaviour, in the ability to complete activities of daily living, and in emotion and affect. The result is that the person with Alzheimer's disease may be more able to support themselves in their own home for longer, or their carer may feel better equipped to continue in their role, thereby delaying entry into residential aged care facilities.

People with Alzheimer's disease and their carers are typically a highly vulnerable group. The patient generally has difficulty communicating as a result of cognitive decline and often lacks legal capacity. They may thus be unable to express themselves and report on outcomes of treatment, and rely on their carer, family, health professional or other trusted person to act as their advocate. As Alzheimer's disease and dementia is typically an age-related condition and because it has such a profound impact on function, people with the disease are mostly unable to maintain employment. Their carer may also be out of the workforce due to their age or the demands of their caring role. If people with Alzheimer's disease are no longer able to access PBS-subsidised treatment, there is a real risk that people who may benefit

will be unable to commence therapeutic treatment or will discontinue treatment due to lack of affordability. The result is a lost opportunity for the person with Alzheimer's disease to trial the anti-dementia drugs and determine if there is symptomatic improvement, and a risk that a patient previously undergoing therapeutic treatment experiences rapid and distressing decline following discontinuation of treatment.

These possibilities are demonstrated in the case studies included as an Appendix to this submission.

The RACP notes the broader policy context in which this review is taking place. Earlier this year, the Living Longer Living Better aged care reform package was announced with $41.3 million over five years to support GPs to make a more timely diagnosis of dementia, allowing opportunities for earlier medical and social interventions. The House of Representatives Standing Committee on Health and Ageing is also currently undertaking its Inquiry into Dementia: Early Diagnosis and Intervention, which includes in the Terms of Reference how early diagnosis and intervention can improve quality of life and assist people with dementia to remain independent for as long as possible.

There is some evidence that anti-dementia drugs may be more effective where there is early and accurate diagnosis of Alzheimer's disease as it may help stabilise the person and allow them to remain living in the community for longer. The PBAC review must ensure that it is aligned with the broader policy context and the public interest of supporting people with dementia to have the highest possible quality of life, and delaying entry into residential aged care facilities.

Recommendations

The RACP make the following recommendations to PBAC:

1. The anti-dementia drugs included in the review should not be removed from the PBS at this time.

2. Continuation of anti-dementia drugs for people with Alzheimer's disease should be authorised where there is either:
   a. A two-point improvement in MMSE score from baseline (or using a comparable tool); and/or
   b. A specialist report recommending continuation that is based on clinician judgement from regular observation and consultation; carer report of improved patient outcomes; and the administration of an appropriate global assessment tool.

Efficacy of the Mini-Mental State Examination for measuring improvement in patients with dementia treated with these medicines

The Mini-Mental State Examination (MMSE) is generally considered to be an effective screening tool to detect cognitive impairment. It is evidence-based with demonstrated reliability and validity. There are, however, documented concerns that the MMSE has limitations including being a largely language-based tool – and thus potentially inappropriate for patients from culturally and linguistically diverse backgrounds (CALD) – with poor ability to detect mild cognitive impairment. In addition, as it is primarily a screening tool, the RACP is concerned that the MMSE is not sufficient for measuring changes or improvement in

cognition and function following intervention nor for determining the efficacy of therapeutic treatment.

The RACP understands that there are a number of dementia assessment tools available to assess cognition, such as the Addenbrooke's Cognitive Examination – Revised (ACE-R) and the Rowland Universal Dementia Assessment Scale (RUDAS), as well as more global measures to assess general functioning including the Clinician's Interview-Based Impression of Change (CIBIC). The RUDAS is particularly advantageous as it was specifically developed for the Australian context for CALD populations who are disadvantaged by the MMSE. Clinicians may use a variety of tests depending on the needs of the patient but the tests may not provide comparable results. For example, a patient may not show improvement on the MMSE but may do so on the ACE-R.

Currently, initial PBS-subsidised treatment of Alzheimer's disease with anti-dementia drugs is authorised for up to six months where the patient has a baseline MMSE score of 10 or more. Continuing PBS-subsidised treatment requires a demonstrated two-point increase on the MMSE score from baseline.

The sole utilisation of the MMSE to measure improvement in patients treated with anti-dementia drugs is problematic because of the limitations described above and because it does not assess the full range of patient outcomes that may be experienced following therapeutic treatment. As demonstrated in the case studies in the Appendix, there are a multitude of cases whereby a patient has not shown improvement on the MMSE but the carer and clinician have reported significant (and often subjective) outcomes including functional and social improvements including increased interaction and reduced aggression and behaviours of concern.

In addition, the nature of Alzheimer's disease and other dementias is that they are characterised by progressive cognitive decline. As such, the score for a person with Alzheimer's disease on the MMSE is expected to decline by about 2-3 points per year. If after six months, the person's score remains at baseline or improves by only 1 point, this could still be considered an improvement and signify that ongoing therapeutic treatment is warranted.

The RACP considers that a clinician assessment combined with carer report is the most effective means of identifying and measuring improvements following therapeutic treatment. As such, the RACP recommends that continuation of PBS-subsidised treatment for people with Alzheimer's disease should be authorised where there is either:

a. A two-point improvement in MMSE score from baseline; or
b. Where a clinician report recommends continuation and that report is based on clinician judgement from observation and consultation, carer report of improved patient outcomes, and the administration of a global assessment tool, such as the CIBIC.

Evidence on the safety and efficacy of anti-dementia drugs

The RACP acknowledges the substantial body of evidence relating to the safety and efficacy of anti-dementia drugs as published in the literature and demonstrated through randomised controlled trials and the Cochrane reviews. Randomised controlled trials are "the most

rigorous way of determining whether a cause-effect relation exists between treatment and outcome and for assessing the cost effectiveness of a treatment."[1]

In this respect, the evidence is clear that anti-dementia drugs are only effective for a subset of patients with Alzheimer's disease and, where effective, demonstrate only modest improvements overall in terms of cognition, behaviour and function.

However, following discussions with PBAC, the RACP considers there is utility in providing information to PBAC about clinicians experience with respect to the safety and efficacy of anti-dementia drugs. The RACP requested this information from our Fellows and the results from this request are included as an Appendix to this submission.

The RACP has reviewed these contributions and, on balance, recommends that the anti-dementia drugs included in the review should not be removed from the PBS at this time.

It is the RACP's opinion that although overall there may only be modest improvements; for a large number of people with Alzheimer's disease, therapeutic treatment is associated with meaningful outcomes for both the patient and their carer, leading to higher quality of life and, possibly, increased ability to remain at home for longer. For people with Alzheimer's disease and dementia – diseases associated with progressive cognitive decline – any form of improvement is rare and there are very limited effective treatment options and currently no cure. As a result, any form of treatment that has the potential to improve outcomes, even for a small number of people, should be made readily available so long as it is safe.

Anti-dementia drugs can be considered safe. Some patients do experience adverse effects and dose-related side effects following therapeutic treatment, however, these can be minimised by starting at a lower dose and slowly increasing according to tolerance. It is important to note here that a patient may tolerate one cholinesterase inhibitor but not others and that memantine can be prescribed where a patient does not tolerate cholinesterase inhibitors. Therefore, all anti-dementia drugs included in this review should remain on the PBS.

For people with Alzheimer's disease, it is important that anti-dementia drugs remain on the PBS so that they are affordable as financial hardship is common and the effect of discontinuing treatment can be severe. As demonstrated in the case studies attached, a number of clinicians reported rapid deterioration in the patients function, language and behaviour following discontinuation of therapeutic treatment and a failure to return to baseline once treatment was reinstated. Continued investment in research is necessary to determine the cause of this decline but, until more is known, the RACP considers the anecdotal evidence sufficient to warrant ongoing access to anti-dementia drugs for people with Alzheimer's disease who are currently undergoing therapeutic treatment and demonstrate improvement in their cognition or function as reported by their clinician and carer.

Conclusion

The RACP would be pleased to provide further information to PBAC about the utilisation and efficacy of anti-dementia drugs. We consider that the depth and breadth of information received during the RACP's consultation process demonstrates the complexity of the issue. We would be willing to undertake further work with PBAC and the Australian Government to

explore options to ensure that people with dementia can access therapeutic treatment in a manner that is both appropriate to their need and cost-effective.

About the RACP

The Royal Australasian College of Physicians (the RACP) trains educates and advocates on behalf of more than 13,500 physicians – often referred to as medical specialists – and 5,000 trainees, across Australia and New Zealand. The RACP represents more than 25 medical specialties including paediatrics & child health, cardiology, respiratory medicine, neurology, oncology and public health medicine, occupational and environmental medicine, palliative medicine, sexual health medicine, rehabilitation and addiction medicine. Beyond the drive for medical excellence, the RACP is committed to developing health and social policies which bring vital improvements to the wellbeing of patients.

References

[1] Sibbald, B. & Roland, M. (1998). Understanding controlled trials: Why are randomised controlled trials important? *BMJ* 316:201.