The Society of Hospital Pharmacists of Australia
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PBS Post Market
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Dear Sir / Madam

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

SHPA is the national professional organisation for nearly 3,000 pharmacists, pharmacists in training, pharmacy technicians and associates working across Australia's health system. SHPA is the only professional pharmacy organisation with a core base of members practising in public and private hospitals and other health service facilities. These pharmacists work within healthcare teams with a focus on supporting the safe and effective use of medicines as their core business.

SHPA supports the decision-making processes of the Pharmaceutical Benefits Advisory Committee (PBAC) including the need for post-market review, and notes the current restrictions to access to donepezil, rivastigmine, galantamine and memantine through the Pharmaceutical Benefits Scheme (PBS).

SHPA and our members have always supported the use of evidence-based treatment guidelines for the introduction and ongoing use of medicines. We acknowledge that the use of cholinesterase inhibitors to treat the symptoms of Alzheimer's disease presents particular challenges as:

- the diagnosis of Alzheimer's disease can be problematic and patients present at different stages of the disease
- a trial with the medicine(s) is required to identify individual patients that benefit from these medicines and which patients can tolerate treatment
- the focus is on symptom control rather than achieving a cure or preventing disease progression; there is no unambiguous measure for effectiveness and for this reason changes in ratings / scores are used to measure improvement and guide continuance of therapy
- the 'real' effectiveness of the medicines in an individual patient can only be fully identified if the medicine is ceased which is not a clinically appropriate option

In addition, the current requirements that must be met for patients to access these medicines through the PBS is onerous and anecdotally leads to treatment failure as continuity of treatment is difficult in many instances

Feedback from our members can be summarised as: **rather than being over used, many patients with Alzheimer's disease who would benefit from these medicines are not receiving treatment** and **long term access through the PBS should be maintained for all patients who have responded to, and are tolerating, these medicines.**

SHPA believes the Department will receive numerous examples of issues relating to the use of these medicines from a range of clinicians. For this reason we have focused our comments on detailing the principles that should drive the availability and clinical use of these medicines.

Eligibility criteria

SHPA believes that the current eligibility criteria, which includes a minimum two point improvement in Mini-Mental State Examination (MMSE), is challenging and excludes many patients but understands the evidence base for the criterion. However we note the current eligibility criteria do not take into account the variability in presentation between patients, various types of dementia and complicating factors such as language, learning and education and communication difficulties.

The management of Alzheimer's disease is about managing deteriorating patients, so the classification of patients as 'responding to treatment' needs to include those who have experienced an improvement in MMSE and those whose MMSE has not declined and / or have shown an improvement in other areas e.g. Alzheimer's disease Assessment Scale (Cognitive sub-scale).

Complexity of starting therapy and ensuring ongoing supply

The complexity of prescribing these medicines in the first six months of treatment through the PBS, including the need for initial written authority (with or without two months of telephone approved therapy) and the continuation rule, sometimes lead to discontinuity of therapy or premature cessation of therapy prior to assessment of benefit at six months.

Initial reviews should focus on dose titration (particularly for rivastigmine which often requires very slow titration over eight weeks) and tolerance of the medicines' side effects. The evidence base suggests a trial of 26 weeks of therapy is required to assess benefits; therefore the impact of the medicine for 'approval' or funding should not be assessed during this period.

These medicines should only be reviewed or withdrawn under supervision of a specialist in this field and after discussion of the risks and reasons for doing so with the patient or carer. Cessation of therapy due to complex approval and funding systems is unacceptable.

Our members have reported cases where patients who are started on therapy in hospital or in outpatient clinics run out of their medicines after one to two months, or at six months because of: administrative issues (e.g. lost postal authority scripts); poor handover between clinicians; poor or miscommunication to patients and/or carers about plans and requirements for ongoing prescribing and supply, failure to make referrals for follow-up, and/or failure to properly document or communicate initial diagnoses and MMSE scores.

Explaining to patient and their carer the process for qualifying for the medicine through the PBS, the use of the hard copy authority prescription and obtaining supplies of these medicines is important to ensure ongoing use, however even a simplified explanation tailored to the patient is too complex for most to comprehend. Examples of where there are considerable problems and confusion for the patient or carer include: when the prescriber has not provided the required information on the prescription, or when the patient is admitted to an aged care facility for temporary care (i.e. transition care program or respite) and the 'usual' prescriber does not order the medicine and medicines are provided by a different pharmacy.

Some of these issues are related to the 'healthcare system' and are not unique to the prescribing of cholinesterase inhibitors, but the complexity of the PBS rules for these medicines certainly contributes to some patients either having breaks in therapy or stopping therapy prematurely. This is not good clinical practice and is associated with rapid decline in mental function, often not reversible even on recommencement and increased risk of adverse effects when re-commencing therapy. It can be particularly detrimental if the deterioration in mental function impacts on the patient's capacity to live independently.

Long-term therapy with cholinesterase inhibitors

The National Institute for Health and Clinical Excellence in the UK has updated its guidance document three times in the last seven years and addresses the issue of determining efficacy of these medicines at length.[1] The guidance is quite clear that evidence of efficacy must be sought using a variety of tools that would examine cognitive, global, functional or behavioural symptoms and that the carer's views on the progress of the patient's condition is essential in the assessment of efficacy.

Although a 2004 Australian study investigating the use of cholinesterase inhibitors in Australia concluded that the institutionalisation rates observed in the cohort of patients "do not seem substantially better than those reported internationally" this cohort included all patients who initiated therapy, it did not report specifically on patients that received more than six months therapy.[2]

A recent double-blind placebo-controlled trial involving community-living patients with moderate or severe Alzheimer's disease already receiving treatment with a cholinesterase inhibitor showed there were modest cognitive and functional benefits of continuing donepezil over a 12 month period.[3] The results of the DOMINO trial may help to explain the 'unexpectedly high' continuation rate for these medicines in Australia.

As noted in an editorial published with the study[4] the results should not be "interpreted as evidence of the efficacy of indefinite treatment with donepezil" however, "the trial results may be viewed as supporting the decisions of patients, caregivers, and physicians who are reluctant to discontinue donepezil because they fear that there is more to lose than gain."

The editorial also notes that the group that discontinued the donepezil recorded an average MMSE score 1.9 points lower than the group that continued the donepezil is "potentially important because many of the patients were severely impaired, on the cusp of needing nursing home care, and slightly worse cognitive function could affect their ability to remain at home."

SHPA agrees with these sentiments. **The risk of losing even a small level of function, that can significantly affect quality of life, is very real for this patient group.**

Given that the intent of therapy is to manage or improve symptoms rather than cure, the 'red tape' that must be worked through to gain access to the medicine, the side effect profile of these medicines and the relatively high cessation rate on initiation of therapy; SHPA believes that patients, caregivers and physicians generally make the decision to continue cholinesterase inhibitors on the basis of clinical need.

SHPA believes that these medicines should be assessed for funding on a similar basis to other medicines that provide symptom control and require ongoing monitoring and review, for example pain control or the use of anti-retrovirals. Initial access should be streamlined and ongoing access supported by the funding rules.

As noted earlier SHPA supports an evidence-based approach to the use of medicines, this includes the discontinuation of medicines. Safe deprescribing of medicines towards the end-of-life should be routine and is particularly important in degenerative diseases where the goals of therapy change throughout the progression of the disease. SHPA would encourage the promotion of algorithms for the deprescribing of medicines.[5]

In summary SHPA believes the current criteria for access to cholinesterase inhibitors through the PBS are adequate to determine funding eligibility and further restriction on access would deny treatment to patients who would benefit from these medicines and cause further unintentional (or unnecessary) discontinuation of therapy or increase treatment failures.

Please contact Karen O'Leary via email: shpa@shpa.org.au if you require any further information about how SHPA may assist to improve the use of cholinesterase inhibitors to treat the symptoms of Alzheimer's disease.

Yours sincerely,

Sue Kirsa

SHPA Federal President

1. http://www.nice.org.uk/nicemedia/live/13419/53619/53619.pdf
2. Le Couteur, D. G., Robinson, M., Leverton, A., Creasey, H., Waite, L., Atkins, K. and McLachlan, A. J. (2011), Adherence, persistence and continuation with cholinesterase inhibitors in Alzheimer's disease. Australasian Journal on Ageing. doi: 10.1111/j.1741-6612.2011.00564.x
3. Howard R, McShane R, Lindesay J et al. Donepezil and memantine for moderate-to-severe Alzheimer's disease. New England Journal of Medicine. 2012 366; 893-903
4. Schneider LS. Discontinuing donepezil or starting memantine for Alzheimer's disease. New England Journal of Medicine. 2012 366: 957-9
5. James E Hardy, Sarah N Hilmer. Deprescribing in the Last Year of Life. Journal Pharmacy Practice and Research 2011; 41: 146-51