

NHS Quality Improvement Scotland

Dear Miss Brownlee

Thank you for the opportunity to comment on the Technical Appraisal for the Cholinesterase Inhibitors and Memantine in the treatment of Alzheimer's disease.

There is very limited data on Memantine in the report as might be expected. However, since the majority of clinical use of Memantine appears to be in conjunction with a cholinesterase inhibitor after a reasonably long period of treatment with the latter I think there will be a requirement at some point to look at how Memantine might modify the QALY for each of the cholinesterase inhibitors rather than to provide a QALY for Memantine which is based on a pattern of usage which does not reflect normal clinical practice. Indeed, superficially the QALY for Memantine looks better than those for the cholinesterase inhibitors but yet the period of study and outcome used are quite different. It would be important for this to be made clear in the final report.

The authors make a very detailed case for their use of their "augmented base case". I believe that their decision to increase the starting utility accorded to Alzheimer's disease is correct because the majority of patients who have treatment with a cholinesterase inhibitor commenced in clinical practice are functioning above the mean of the subjects reported in the key note double blind placebo controlled trials.

In addition, the concentration on the benefit to patients who are not in full time care at the end of 5 years treatment is to be welcomed. Many clinicians have argued that the current NICE/HTBS Guidance on the Use of Cholinesterase Inhibitors is flawed by its concentration on short term primarily cognitive response rather than a delay in the onset of severe dementia which is of more clinical value.

The absence of alteration in carer utility is interesting and the point will no doubt be argued by carer organisations. Nonetheless, the authors identify the lack of evidence for carer effect associated with cholinesterase inhibitor treatment and it would be useful for the final NICE Guidance to recommend exploration of carer benefits as priority for further research. Indeed the point could be argued that there is very little literature which quantifies carer benefits for most interventions and this could point could be made as a generic comment.

The changes in patient utility are much more dramatic than those in carer utility. Whilst the implication is that it is the patient who stands to gain most benefit from the use of cholinesterase inhibitors (which is a laudable statement) in reality benefit is often measured by a composite effect on the patient and carer. Whilst I suspect that there may be methodological difficulties and that the final QALY results may not change it would be useful if the authors were able to provide information on a QALY derived from composite patient/carers indices which they have used in their analysis.

Whilst the authors have a reasonable case for simply comparing the three cholinesterase inhibitors on a level playing field clinical use is not quite so straightforward. The action of Donepezil makes it far more likely that patients who are living alone will be receiving

NHS Quality Improvement Scotland

Donepezil rather than Rivastigmine or Galantamine. If it was possible for this to be quantified and reflected in the economic analysis it appears to me that the final conclusions would be a bit more robust.

I do not know whether I am allowed to see other comments which are made on the paper but I would certainly be interested if it was possible. In the meantime I have mailed the confidentiality agreement to you.

Kind regards.

Yours sincerely

Peter J Connelly
Consultant Psychiatrist

20/01/05