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Dear Kate Moore

Re: Health Technology Assessment: donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (TA 111)

Comments on appraisal consultation document by the Faculty of Old Age Psychiatry, Royal College of Psychiatrists.

Thank you for sending this document for comments. The Faculty of Old Age Psychiatry very much welcomes the proposed change in guidance to now allow use of all three cholinesterase inhibitors and memantine within their licensed indication. As you will know, we previously fundamentally disagreed with the previous NICE Guidance limiting these drugs, and the economic analysis on which this was based, and are now pleased to see that the drugs are felt to be highly cost effective. This change will significantly improve the management of Alzheimer's disease within the UK, and bring us more into line with clinical practice in other countries.

I would suggest the following modifications be considered by the committee.

1. The recommendation remains for six monthly monitoring, yet there is no evidence base for this. In practice, these drugs are usually continued for two to three years and routine monitoring every six months serves no useful purpose. There is a real danger that, because of increased prescribing and limited NHS resource in the years ahead, a large proportion of resource will be taken up with unnecessary routine monitoring of patients who are otherwise well. We would suggest that the recommendation is changed to "patients who continue on the drugs should be reviewed according to both clinical need and local shared care arrangements". It is noteworthy that there is now a requirement for primary care to undertake reviews of people with dementia and their carers every 15 months.

2. Given that all drugs are now deemed cost effective, then there should be no recommendation that treatment should normally be started with the drug with the lowest acquisition cost. This varies considerably both in geographical location and over time, and will undoubtedly alter again when the drugs come off patent in 2012. There are important differences in drug interactions and side effects between the different agents, as well as in mode of administration and these clinical factors should be the driving force

in choice of agent rather than lowest acquisition cost. It is not unusual for the drug with the lowest acquisition cost to be rivastigmine, which is associated with much higher costs in terms of more frequent monitoring (for dose titration) and also is often associated with more frequent gastrointestinal side effects.

3. There is reference made on many occasions to the lack of evidence for combined benefit of the cholinesterase inhibitor with memantine. At stages of more moderate to severe dementia it may well be appropriate for memantine to be introduced and the two can be safely coprescribed. It might then be appropriate for the cholinesterase inhibitor to be withdrawn, but there may well be a necessary period where a cholinesterase inhibitor is coprescribed with memantine, though comment could be made that this should not be routinely continued in the longer term.

4. There remains a heavy reliance on use of the MMSE to judge dementia severity which is not appropriate. The severity scores are given as if there is some determined truth behind these cut-offs; they are very arbitrary and staging of dementia relies far more on a holistic process which takes into account a patient's functionality, activities of daily living, and neuropsychiatric features, as well as the MMSE score, based on factors including their premorbid education level, extent of concurrent problems such as dysphasia or hearing and visual impairment. We would strongly recommend that the MMSE is not used as a means for determining eligibility for cholinesterase inhibitors; it is quite sufficient to state that the drugs should be used within their licensed indication.

5. It is also important to note that moving to a residential home or institutionalisation should not necessarily indicate that the stage of severe dementia has been reached and that cholinesterase inhibitors should be withdrawn. There are many factors influencing institutionalisation, neuropsychiatric features and carer stress being two of the most powerful. Neither of these would indicate the need for withdrawal of cholinesterase inhibitors; indeed, if this were the case, then neuropsychiatric features might well worsen.

We hope the committee will take account of these comments at its meeting at the end of November.

With best wishes.

Yours sincerely

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