Alzheimer's Society response to the Appraisal Consultation Document for R111 (October 2010)

Alzheimer's Society welcomes the opportunity to comment on the Appraisal Consultation Document (ACD). We strongly support the recommendations contained in the ACD and recommend that they are upheld in the Final Appraisal Determination. This would represent an important step forward in the development of an effective and comprehensive package of care for people with Alzheimer's disease. It would also support the achievement of the important public policy aim of improving rates of diagnosis and early intervention for people with dementia.

Alzheimer's Society believes there are a number of ways in which the economic modelling could be improved (as discussed below) and these are also likely to improve the cost effectiveness profile of the treatments. We have the following comments to make:

1. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

Alzheimer's Society believes the recommendations within the ACD are a suitable basis for guidance to the NHS.

The review of published evidence carried out to inform this review has confirmed previous systematic review findings[1, 2] that all four of these drug treatments are clinically effective. The ACD also acknowledges that, for a significant proportion of people with Alzheimer's disease, the drugs have benefits that are not likely to be picked up by the standard scales used within clinical trials (para 4.3.7). This conclusion is consistent with the reports of carers and people with dementia that the drug treatments have benefits for many and are an important addition to a comprehensive package of care.

In addition, the review has confirmed that these drugs are cost-effective. Both the manufacturers' and Assessment Group models found the drug treatments to be cost effective, enabling NICE to be particularly confident that the drug treatments represent an effective use of NHS resources. In addition, with regard to memantine, the ACD notes that 'The Committee therefore concluded that the cost effectiveness of memantine may have been underestimated in the

[1] Birks J (2006) Cholinesterase inhibitors for Alzheimer's disease. *Cochrane Database of Systematic Reviews.* Issue 1.

[2] McShane R, Areosa Sastre A, Minakaran N (2006) Memantine for dementia. *Cochrane Database of Systematic Reviews*. Issue 1.

Assessment Group's model for patients with severe Alzheimer's disease, although by how much is uncertain.'

Anticholinesterase drug treatments

We are very supportive of the recommendation to extend prescription of the anticholinesterase drug treatments to people with an MMSE above 20. As we explained in our submission to this review, people with Alzheimer's disease feel very strongly that the goal of anticholinesterase treatment should be the extension of the period during which symptoms are most mild. This is when people are best able to cope with symptoms and retain some independence and quality of life. This is the stage at which a delay in progression is most wanted.

Provision of potentially effective drug treatment in the mild stages of Alzheimer's disease also supports the important policy aims of increasing rates of diagnosis and early intervention. We know that individuals experiencing symptoms often delay seeking help and also that GPs can be reluctant to diagnose dementia because they believe there is little that can be done. The availability of a drug treatment in the early stages is likely to encourage people to seek help from their GPs. It also provides an additional incentive to GPs to diagnose people and refer them to specialist services.

Memantine

Alzheimer's Society is also extremely supportive of the recommendation that memantine should be available as a treatment option to people in the moderate and severe stages of Alzheimer's disease. Memantine is the only licensed and effective drug treatment for people in the severe stages of dementia

As stated in the ACD, published evidence demonstrates that memantine is clinically effective. This is supported by reports to the Alzheimer's Society from people with dementia and carers. Although sometimes it is more difficult to understand the experience of people in the later stages of Alzheimer's, we now know more about the importance of trying to maintain quality of life throughout the course of dementia. Many people have reported to us that prescription of memantine has resulted in important and meaningful benefits, for example being able to use the toilet unaided.

The improvements that memantine can bring to behavioural symptoms are particularly important, as these are the symptoms that can be most distressing to people with dementia and their carers.[3] We discuss under section 2 the consideration given to behavioural symptoms by the Appraisal Committee. The

[3] Deimling GT and Bass DM (1986) Symptoms of mental impairment among elderly adults and their effects on family caregivers. *Journal of Gerontology.* 41:778-84.

reliance on anti-psychotic drugs as a treatment for behavioural symptoms highlights the importance of having a clinically and cost effective treatment, that has none of the serious side effects of antipsychotic drugs, available on the NHS. The reduction of antipsychotic prescription by two-thirds by November 2011 is a clearly stated public policy aim and this NICE recommendation will provide helpful support to achieving this aim.

2. Has all of the relevant evidence been taken into account? Are the summaries of clinical and cost-effectiveness reasonable interpretations of the evidence?

We support the conclusion that the four drugs are clinically and cost effective. We also believe that the current Assessment Group model improves upon the SHTAC model in important ways. We particularly welcome the acknowledgement that there is heterogeneity of costs and quality of life in the pre-full time care state. However, there are still a number of acknowledged limitations and we feel it would be important to work together to achieve an improved consensus model for future appraisals.

It is disappointing that, as the ACD acknowledges, 'important gaps in the evidence remain'. Some of these gaps will pertain to further improvements of the model as suggested above. For example, the evaluation still fails to acknowledge the benefits the drugs can provide to carers. We recognise that there is limited data on this and that carer benefit was included in a sensitivity analysis. However, given the significant burden on carers of people with dementia and the increased risk of psychological morbidity and reduced quality of life,[4] we believe it is important to develop methods for incorporating any benefits to carers. We still believe that in the absence of any good data on carer quality of life, methods should be developed to incorporate the findings from clinical trials that the drug treatments can reduce the time carers spend caring.

It is also disappointing that there are no data from clinical trials on quality of life for carers and for people with Alzheimer's disease, and also with regard to service use. We recognise that it is unlikely these issues will be addressed for currently licensed drugs as they will soon be going off patent and there will be limited further trials. We do however agree it would be extremely important to make recommendations that trials for new emerging treatments do address these issues.

However, there are other sources of evidence addressing quality of life. We welcome the Appraisal Committee's recognition of patient evidence of the benefits of treatment. As noted, these benefits may not be captured in scales

[4] Moise P, Schwarzinger M, Um M-Y (2004) *Dementia Care in 9 OECD Countries: A Comparative Analysis.* Paris: DELSA/ELSA/WD/HEA.

normally used within clinical trials but can be very meaningful in the context of people's day-to-day lives (para 4.3.7.). It is important to use the personal accounts of individual experience with the drug treatments alongside data from clinical trials to develop a better understanding of their benefits.

Because of the lack of up to date evidence on patterns of service usage, the Assessment Group has had to rely on out of date and limited data from the Wolstenholme study. We believe that using more up to date evidence would result in the drug treatments appearing more cost-effective as the differential between costs in the early and severe stages would be greater – in 2010 people do not receive services until their needs are greater and individuals entering institutions have a higher level of need.

As acknowledged in para 4.2.23 the failure to assume a treatment benefit in behavioural and psychological symptoms is a limitation of the model. This is particularly a problem for memantine. Amelioration of these symptoms is one of the most important benefits of the drug and we note the Committee's conclusion in para 4.3.13 that 'on the basis of the manufacturer's evidence and clinical specialist testimony that memantine appears to have an effect on these symptoms.' As noted in our submission, we would like to see work carried out to develop a model that uses available data to capture the contribution of MMSE score, NPI score (including key symptoms such as agitation/aggression, psychosis, depression and apathy) and functional ability to quality of life and costs. It is particularly important to incorporate behavioural symptoms into a model because of the evidence of their impact on costs.[5]

Alzheimer's Society would also like to see risperidone used as a comparator for the treatment of behavioural symptoms. Risperidone is licensed for the "short-term treatment (up to six weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others". Although the response to behavioural and psychological symptoms should be individualised and based on good person centred care the reality is that antipsychotics are widely used as the first-line treatment.

Additional comments

The Audit Support Guidance for TA111 makes it clear that 100% of people with moderate Alzheimer's should be considered for treatment with one of the anticholinesterase drugs. We would welcome a similar audit standard to be established for the revised guidance. This would be an important driver to

[5] Murman DL, Chen Q, Powell MC, et al (2002) The incremental direct costs associated with behavioural symptoms in Alzheimer's disease. *Neurology.* 59: 1721-9.

encourage local areas to increase rates of diagnosis of Alzheimer's disease, which remain unacceptably low.[6]

In light of the well-recognised problems in recognising and responding appropriately to symptoms of Alzheimer's disease we would welcome the opportunity to work with NICE on communicating the revised guidance to GPs and other healthcare professionals, should the ACD remain unchanged. We believe the recommendations as they stand would act as an incentive to GPs to refer people to memory assessment services for diagnosis and access to a range of support, including potential treatment with one of the four licensed drugs. The value to people with dementia of having access to an effective memory assessment service that offers a comprehensive service is recognised within the NICE Quality Standards. The recommendations within the ACD would help to support the achievement of these standards.

[6] National Audit Office (2007) *Improving Services and Support for People with Dementia.* NAO