

NICE recommends drugs for moderate Alzheimer's disease

Susan Mayor *London*

Cholinesterase inhibitors for Alzheimer's disease should be considered in the treatment of patients with moderately severe disease but not for those with milder symptoms, says revised draft guidance issued this week for the NHS in England. The guidance follows a review of a first draft that had advised against the use of these drugs at all in the disease.

The latest guidance recommends that donepezil, galantamine, and rivastigmine should be considered in the treatment of people with Alzheimer's disease of moderate severity, defined as those with a minimal state examination score of 10-20 points.

Memantine, an N-methyl-D-aspartic acid antagonist, was not recommended as a treatment option for people with moderately severe or severe Alzheimer's disease except as part of clinical studies. The guid-

ance was issued by the National Institute for Health and Clinical Excellence (NICE), the body that advises on the use of treatments by the NHS.

The original NICE guidance on the use of donepezil, galantamine, and rivastigmine for Alzheimer's disease, issued in 2001, recommended that their use should be considered in all patients but should be stopped as soon as they no longer had an effect.

The organisation's first draft review of this guidance, issued in March 2005 (*BMJ* 2005;330:495), found insufficient evidence to support the use of these drugs for any patients and therefore advised that they should no longer be prescribed by the NHS. Patients already on the drugs could remain on them, however.

Responses to the first draft from stakeholders, including groups representing people with

the disease and doctors working in the field, argued that the drugs may be effective for certain groups of people. NICE therefore asked the drug companies involved in the appraisal to look for evidence to support this argument from the data in their clinical trials.

After reviewing this new evidence, together with data seen previously, the NICE appraisal committee concluded that donepezil, galantamine, and rivastigmine were clinically and cost effective in patients with moderate Alzheimer's disease—around 40% of patients with the disease. It did not recommend the use of memantine, because there was insufficient evidence of its clinical benefit for patients with moderately severe or severe Alzheimer's.

The revised draft guidance has been published on the NICE website (www.nice.org.uk) for a three week public consultation period ending on 13 February. Final guidance is expected in July 2006. In a statement NICE said that the original guidance would apply until updated guidance is finalised. When it is published, the guidance will apply only to

patients with newly diagnosed disease. "Patients currently using these drugs should continue to do so on the basis on which they were initiated," it said.

Andrew Dillon, NICE's chief executive, said: "We are acutely aware of our responsibility to help people with Alzheimer's disease secure access to effective treatment. We needed to make the right decision, based on all the relevant evidence. By going the extra mile and asking the drug companies to delve deeper into their clinical trial data, we have been able to identify the right way to use these medicines."

The drug companies Eisai and Pfizer, which jointly market donepezil, welcomed NICE's revised position but said, in a statement, that the institute had missed the opportunity to highlight the value of earlier treatment with the drugs in mild Alzheimer's disease. Tony Elliott, professor in mental health of later life at the Centre for Ageing and Mental Health at Staffordshire University, said: "Clinically it makes sense to treat patients as early as possible in what is a progressive deteriorating illness." □

US Supreme Court upholds Oregon's Death with Dignity Act

Fred Charatan *Florida*

In a 6-3 decision the US Supreme Court last week upheld Oregon's law on doctor assisted suicide. The dissenters were the chief justice, John Roberts, and judges Anthony Scalia and Clarence Thomas. The ruling said the 1997 Oregon law, which allows doctors to end the lives of terminally ill people who ask for it, trumped federal authority to regulate doctors.

This was a setback for the Bush administration's attempt, in a case called *Gonzales versus Oregon*, to punish doctors by prosecuting them for violating the federal Controlled Substances Act of 1970.

In 2001 the attorney general, John Ashcroft, called doctor assisted suicide "not a legitimate purpose" for prescribing drugs



Scott Rice, whose wife used Oregon's assisted suicide law to end her life, holds up a sketch of the Supreme Court hearing

and vowed to prosecute Oregon doctors he said were violating the law.

But in 2004 a federal appeals court ruled that in passing the Controlled Substances Act Congress did not give the attorney general the unilateral authority to penalise doctors who followed state law in prescribing federally regulated drugs (*BMJ* 2004;

328:1337). That was also the position taken in 1998 by Janet Reno, the attorney general in the Clinton administration.

The appeals court said that the federal law on drug control was intended to halt drug traffickers, not to regulate doctors or the practice of medicine. Historically, the licensing of doctors and regulation of medicine have

been left to the individual states.

The Death with Dignity Act was approved twice by Oregon's voters and took effect in 1997. The law requires that patients wanting to die must have a life expectancy of less than six months, as determined by two doctors; must be mentally competent and not suffering from impaired judgment resulting from depression or another psychiatric disorder; must make an initial request to the doctor and then wait 15 days before making a written request that is witnessed by two people; and must be advised of all alternatives, such as hospice care and pain management. The doctor then prescribes the drugs but may not administer them. As of the last reporting period in 2004, 326 patients had received prescriptions and 208 actually used the drugs to end their lives.

The most commonly reported reasons given for assisted suicide between 1998 and 2004 were loss of autonomy (cited in 87% of cases), decreased ability to participate in activities that make life enjoyable (84%), and loss of dignity (80%). □