Cost Effectiveness of Memantine in the Treatment of Moderately Severe and Severe Alzheimer's Disease in Norway

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Abstract

Placebo-controlled clinical trials have demonstrated the efficacy of memantine versus placebo in moderately-severe and severe Alzheimer's disease. A modelling approach has been adopted to estimate costs and outcomes of memantine treatment in clinical practice in Norway. A Markov model simulated moderately-severe and severe patients' progression through levels of combinations of severity, autonomy and setting over 5 years. Model inputs include clinical trial results and measurement of patient and caregiver resource utilisation from a societal perspective using literature and expert data. The main outcome measures are time spent in autonomy (patient's ability to accomplish activities using the ADCS-ADL scale) and time to institutionalisation.
The time spent in autonomy for patients treated with memantine is 12% longer in duration than for patients treated with donepezil and 24% longer than for patients without pharmacotherapy. Time to institutionalisation is 7% longer with memantine compared to donepezil and 11% longer with memantine compared to no treatment. Over a 5-year period, patients treated with memantine showed a decrease of €5,979 and €12,364 in total healthcare costs, compared to donepezil and no treatment, respectively. Robustness of the results was validated by a comprehensive sensitivity analysis.
In conclusion, memantine is more effective in increasing time spent in autonomy and in reducing healthcare costs compared to donepezil or no pharmacotherapy.

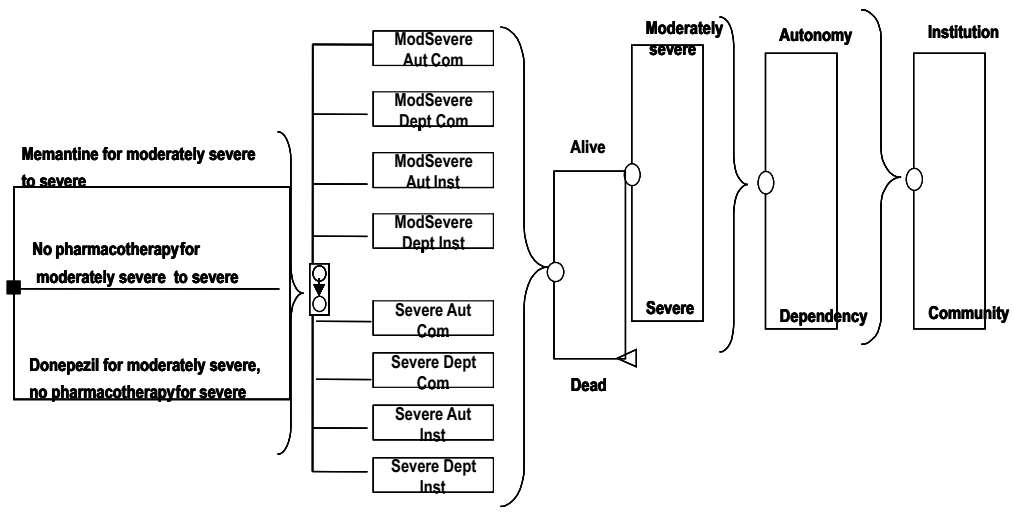
Introduction

Memantine is an uncompetitive N-methyl D-aspartate (NMDA) receptor antagonist, which selectively blocks pathological sustained activation by glutamate while allowing the normal physiological function of the NMDA receptor. It is the first molecule having demonstrated a clear clinical benefit in the treatment of moderately severe and severe Alzheimer's Disease (AD), as stated by the European Agency for the Evaluation of Medicinal Products (EMEA) (1).
A resource utilisation analysis was performed alongside a double blind, randomised, placebo-controlled study. This 28-week assessment conducted in the United States compared resource utilisation and costs for patients receiving memantine with those receiving placebo. The analysis showed that in the US, patients treated with memantine needed less caregiver time (difference 51.5 hours per month; 95% CI -95.27, -7.17; p=0.02), trended to be institutionalised later (p=0.052) and cost less compared to patients receiving no treatment (difference $US 1089.74 per month; 95% CI - 1954.90,-224.58 p=0.01) (2). As management of Alzheimer's disease is country specific, a modelling approach has been adopted to assess the potential cost and effectiveness impact of memantine as compared to standard care (donepezil or no treatment) in the treatment of moderately severe to severe AD in Norway.

Methodology

A Markov model simulated the progression of Norwegian AD patients through levels of a combination of severity, dependency and setting over 5 years. Within a series of 6-months cycles, patients may move from one state to another based upon a predetermined set of transitional probabilities.

This model was composed of 3 treatment arms:
- memantine 20 mg for moderately severe to severe AD patients,
- no pharmacotherapy for patients in the same categories,
- donepezil (5-10 mg) for patients with moderately severe AD followed by no pharmacotherapy when patients reached the severe AD stage.



- The primary outcome measure is 'time to dependence' which was based upon patient dependency. Non dependency was defined by a patient's ability to accomplish the basic and instrumental activities of daily living (ADL) and was measured by standardized ADL assessment tools (modified ADCS-ADL) Sufficient non dependency corresponds to a patient that is able to perform basic activities (eating, bathing, dressing..) as well as instrumental activities (walking, using the phone, watching TV..).
  The secondary outcome measures are the time to institutionalisation. The model also combines the outcomes rates (as just defined above) and costs to calculate the cost-effectiveness ratios expressed in terms of costs per incremental year in autonomy and cost per incremental year when living in the community.
- In the memantine and placebo arms, transition probabilities came mainly from clinical trial data (3). Transition probabilities in the donepezil arm were those previously used in a published modelled economic evaluation by Stewart et al.(4), which evaluated the use of donepezil in the treatment of mild to moderate AD patients. However, when patients transited to the severe stage, donepezil was discontinued because donepezil is not indicated for severe AD patients and probabilities of the placebo arm were applied.
- The probability of death came from literature (4).
- Resource use per MMSE score was based on a Danish cohort (6), assuming that the Danish and Norwegian populations are representative of each other. Expert panel confirmed the validity of this assumption.
  Unit cost data were derived from official tariffs and locally collected information.
- At the start of treatment the cohort is composed of moderately severe and severe AD patients as determined by epidemiological data (5). Within the moderately severe to severe population, 48% of patients are moderately severe and 52% severe. The evaluation is made for this distribution, assuming that all patients are autonomous and live in the community.

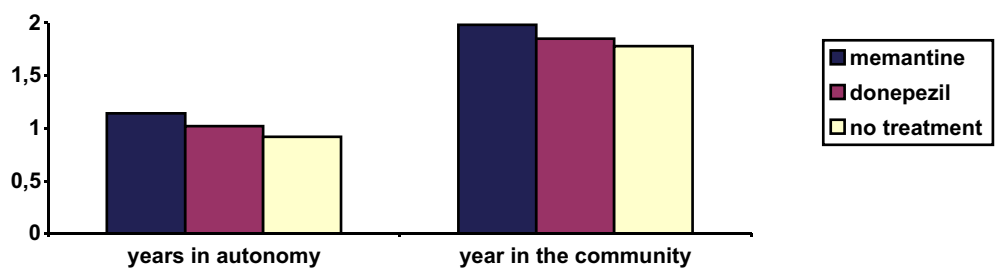
Table 1: Mean 6-month Cost per Patient (€)

State	Community		Nursing Home	
	Autonomous	Dependent	Autonomous	Dependent
Moderately severe	6,860	10,490	28,070	46,450
Severe	10,990	26,450	33,090	33,340

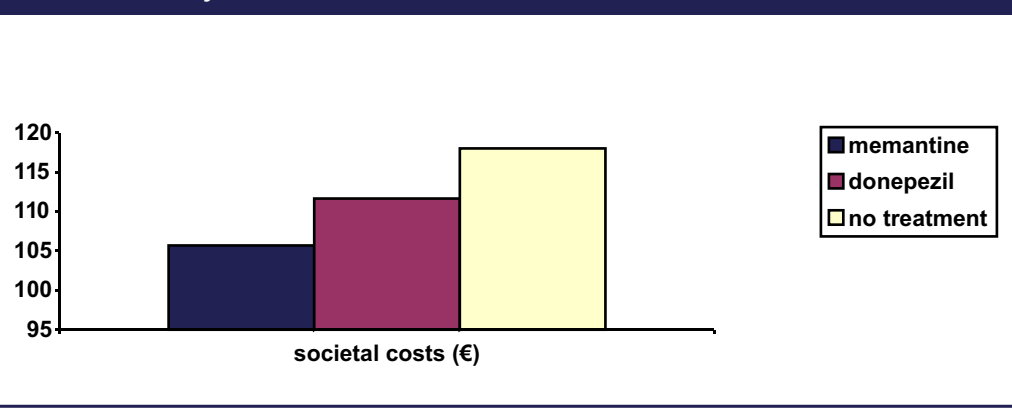
RESULTS

The time spent in autonomy for patients treated with memantine is 12% longer in duration than for patients treated with donepezil and 24% longer than for patients without pharmacotherapy. Time to institutionalisation is 7% longer with memantine compared to donepezil and 11% longer with memantine compared to no treatment. Over a 5-year period, patients treated with memantine showed a decrease of € 5,979 and €12,364 in total healthcare costs, compared to donepezil and no treatment, respectively.

Patients benefits over 5 years



Patients costs over 5 years



Robustness of the results was validated by a comprehensive-sensitivity analysis.

Conclusion

Memantine increase years in autonomy and within the community and decreases societal costs compared to donepezil or no treatment. Consequently memantine is not only a cost-effective strategy but offers cost-saving too.

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