

Pharmacologic Management of Dementia in the Hospice Setting



Hospice seeks to relieve suffering and improve end-of-life care by reducing non-beneficial treatments for those patients diagnosed with end-stage dementia. Hospice care for those with end-stage dementia has been proven to improve pain management, provide much needed psychosocial support for the family and caregivers, and reduce hospital days. While pharmacologic means exist for treatment of mild to moderate and moderately severe to severe stages of dementia, the efficacy of these medications for end-stage dementia has not been proven.¹ End-stage dementia is defined as Functional Assessment Staging (FAST) level 7C to 7F corresponding to Hospice Admission Criteria. FAST 7C: Ambulatory ability is lost (cannot walk without personal assistance). 7D: Cannot sit up without assistance (e.g., the individual will fall over if there are not lateral rest arms on the chair). 7E: Loss of ability to smile. 7F: Loss of ability to hold head up independently.

DISEASE FACTS

- More than 30% of women and 20% of men age 65 or older will develop some form (vascular, Lewy Body, multi-infarct, frontotemporal, Alzheimer's) of dementia.²
- An estimated 4.5 million Americans are currently diagnosed with Alzheimer's disease and it is predicted that the number will increase to 16 million by 2050.³
- Financial costs to families are over \$65 billion per year while total cost to society is over \$100 billion per year.⁴
- Medicare costs are 70% higher for patients with Alzheimer's disease compared with those with other diagnoses.⁴
- Aggressive non-comfort directed treatments in the late stages of dementia do not slow disease progression, increase comfort, or extend survival, and in fact possibly hasten the disease progression.⁵
- There is currently no cure for Alzheimer's dementia.

MEDICATION FACTS

- Cholinesterase inhibitors (donepezil, rivastigmine, galantamine) and memantine are the only drugs currently available for treatment of Alzheimer's disease.⁶
- Cholinesterase inhibitors are FDA approved for the treatment of mild to moderate stages of the disease.⁶
- No evidence demonstrates cholinesterase inhibitors are effective in patients with severe or end stage Alzheimer's disease.⁴
- No evidence demonstrates cholinesterase inhibitors or memantine are effective in end-stage Alzheimer's disease as defined by FAST scale 7C and beyond.

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- Memantine may have modest clinical benefits and lead to a slower functional decline with Alzheimer’s disease, but it will not change the overall course of the disease.⁷
- Combination therapy of cholinesterase inhibitors and memantine has only been studied in moderate to severe stages of Alzheimer’s disease.
- No studies have demonstrated an increase in the duration of the positive effects obtained by adding cholinesterase inhibitors or memantine.

Table 1. REVIEW OF MAJOR DRUG TREATMENT TRIALS

Author	Level of Evidence	Sample Population	Study Length	Assessments Used	Summary of Results
Doggrell (2003)	II	252 subjects with moderate to severe AD Drug study for memantine alone	28 weeks	(pre-drug) MMSE, FAST (end points) MMSE, FAST as secondary measurements	Memantine group showed no improvement in MMSE
Reisberg et al. (2006)	II	175 subjects with moderate to severe AD (extension study) Drug study for memantine alone	24 weeks	(pre-drug) MMSE, FAST (level 6a or greater) (end points) MMSE, FAST are secondary measurements	Memantine group experienced significant benefit in all main efficacy assessments (functional, global, and cognitive) versus placebo
Tariot et al (2004)	II	404 subjects with moderate to severe AD Drug study for adding memantine to donepezil	24 weeks	(pre-drug) MMSE (end points) FAST is secondary measurement	Memantine group showed statistically significant benefits in all categories versus placebo
Dantoine et al (2006)	III	202 subjects with moderately severe AD Drug study examining rivastigmine alone & with memantine after failing CI	28 weeks	(pre-drug and end point) MMSE	Rivastigmine alone may improve measures of cognition & behavior or adding memantine when continuing to decline may be helpful

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		therapy			
Winblad et al (1999)	II	151 subjects with severe primary dementia Drug study examining efficacy of memantine	12 weeks	(pre drug) MMSE (end points) CGIC & BGP	Memantine group showed improvement in all areas
Author	Level of Evidence	Sample Population	Study Length	Assessments Used	Summary of Results
Feldman et al (2001)	II	290 subjects with moderate to severe AD Drug study for donepezil	24 weeks	(pre drug) MMSE, FAST (end points) CIBIC – Plus, MMSE	Donepezil showed improvement in all areas

Abbreviations: AD – Alzheimer’s disease, MMSE – Mini-Mental State Exam, FAST – Functional Assessment Staging, CI – cholinesterase inhibitors, CGIC – Clinical Global Impression of Change, BGP – Behavioral Rating Scale for Geriatric Patients, CIBIC-Plus – Clinician’s Interview-Based Impression of Change plus Caregiver Input

Table 2. Level of Evidence Ratings ¹⁵	
Level I	Evidence obtained from systematic review of relevant, randomized, controlled trials with meta-analysis where possible
Level II	Evidence obtained from one or more well-designed, randomized, controlled trials
Level III	Evidence obtained from well-designed, non-randomized, controlled trails OR from well-designed cohort or case-control analytical studies, preferably multi-center or conducted at different times
Level IV	The opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

PSYCHOSOCIAL ISSUES

- Families grieve the patient’s incremental losses of functional ability throughout course of the disease.⁸
- Pharmacologic treatments may provide brief improvement, but the grief process will have to be repeated by the patient and family when treatments inevitably fail.⁸
- Disease prevention or progression delay in the early stages of the disease may be a more desirable goal than attempting to slow disease progression and prolong the morbidity of end-stage disease.⁸

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RECOMMENDATIONS

- The currently available medical literature documents the efficacy of pharmacological treatments in the mild to moderate stages of Alzheimer's disease and for those patients in the moderate to severe stages of disease.⁹
- There are no studies that examine efficacy of pharmacologic treatments in end-stage of the disease as defined by FAST 7C and beyond; FAST 7C: Ambulatory ability is lost (cannot walk without personal assistance). 7D: Cannot sit up without assistance (e.g., the individual will fall over if there are not lateral rest arms on the chair). 7E: Loss of ability to smile. 7F: Loss of ability to hold head up independently.
- The duration of clinically significant benefit is not well established in any group of patients.
- Specifically, there are no well defined clinical endpoints that allow us to know when to stop these medications.
- At the present time it seems prudent to recommend that pharmacologic treatments be discontinued once a patient has declined or disease has progressed while on treatment and/or is determined to be at the end-stage of their disease.
- At the point of discontinuation of these medications, the focus should shift to patient comfort and ongoing social support for the patient and family.

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