

March 6, 2013

Dear Nursing Home Administrator:

The New York State Department of Health (DOH) and the Office of the Medicaid Inspector General (OMIG) seek your cooperation in ensuring the appropriate use of antipsychotic medications for nursing home residents. The Centers for Medicare and Medicaid Services (CMS) recently launched an initiative aimed at improving behavioral health and reducing the use of unnecessary antipsychotic drugs in nursing home residents, an effort that DOH and OMIG fully support. Inappropriate use of these medications in elderly demented individuals is a significant resident safety issue that requires your immediate attention.

The purpose of this letter is to provide you with some resources that may assist your facility in ensuring appropriate care for residents and compliance with federal regulation 42CFR §483.25(l), Unnecessary Drugs (refer to [www.CMS.gov](http://www.CMS.gov), SOM, Appendix PP) with specific emphasis on antipsychotic medications.

Over the last several years, the use of antipsychotic medications has grown exponentially. Published scientific studies document that the use of these drugs in elderly demented individuals is associated with increased morbidity and mortality, with particular associations noted with regard to hyperglycemia, strokes, falls, weight gain, movement disorders (tardive dyskinesia and extrapyramidal symptoms), sedation, blood clots and cognitive decline. The FDA issued a “black box” warning in 2006 about these risks associated with the use of atypical antipsychotic drugs with elderly patients suffering from dementia. Despite the warnings from the FDA and the reports from the research community, antipsychotic medications continue to be used to treat elderly nursing home residents with no prior diagnosis or history of psychosis. Off-label usage of these drugs has continued to increase, and they are now administered to some 21 percent of nursing home residents nationwide, with the vast majority being in contraindication of FDA warnings, as reported by the Health and Human Services Office of Inspector General (HHS OIG) in a report dated May 4, 2011.

The HHS OIG follow-up report of July 6, 2012 found “nearly all records [of nursing home residents receiving atypical antipsychotic medication] reviewed failed to meet one or more Federal requirements for resident assessments and/or care plans.” Multiple reports in the popular press (*Wall Street Journal*, *New York Times*, *Boston Globe*, *Time*, etc.) have excited public apprehension that these medications are being used, in many cases, as a form of chemical restraint, at great cost to taxpayers and great risk to a vulnerable cohort of frail senior citizens.

We are seeking to partner with you to address this important issue to benefit your residents and to assure that these drugs are used appropriately and safely. It is acknowledged that physicians are at liberty to prescribe medications “off-label,” even in conditions covered by

“black box” warnings. However, given the high risks associated with this particular class of drugs, the burden is on the prescriber, as well as the institution allowing the practitioner to care for residents, to ensure that the benefits to be achieved by the prescribing of such medication outweigh the risks involved.

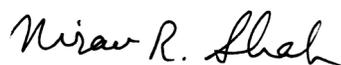
DOH nursing home surveyors are trained and responsible to complete quality reviews for unnecessary medications with an increased focus on, and awareness of the use of antipsychotic medications. Surveyors evaluate, through documentation, interview and observation, such aspects as non-pharmacological interventions, gradual dose reduction when indicated, and interdisciplinary evaluation and review. The nursing home is expected to engage all members of the interdisciplinary team, including the medical director and attending physicians, in the development and review of policies and procedures to ensure that the use of antipsychotic medications promotes and/or maintains the resident’s highest practicable mental, physical and psycho-social well-being. The medical director, in particular, plays a key role in this effort.

To facilitate compliance with Federal Regulations 42 CFR §483.25 (*see* Attachment #1) regarding the avoidance of unnecessary drugs, two protocols are attached for your consideration to use as part of your Quality Assurance and Risk Management programs. The first was the product of working groups of physicians, pharmacists, nurses and senior care specialists from the DOH, OMIG and the Albany Medical Center Alzheimer’s Center. (*See* Attachment #2.) The second was produced by the Partnership to Improve Dementia Care in Nursing Homes, a nationwide consortium headed by the Centers for Medicare and Medicaid Services (CMS). (*See* Attachment #3.) As noted earlier, CMS’ initiative is aimed at reducing the usage of unnecessary antipsychotic drugs in nursing homes nationwide by no less than 15 percent by the end of 2012. (*See* Attachment #4.)

Attachment #5 is “Guidelines for Management of Alzheimer’s Disease and Related Dementias,” published by the National Guideline Clearinghouse of the Agency for Healthcare Research and Quality (AHRQ). Attachment #6 is the “Dear Medical Director” letter from the American Medical Directors Association (AMDA), which you may wish to share with your medical staff.

These attachments are not mandated for adoption, nor does your use of any of these tools guarantee compliance with regulatory requirements. We hope, however, that these resources prove useful to you in your endeavors to assure the highest quality of care for your elderly residents with dementia. We look forward to working with you and thank you in advance for your immediate efforts on this important patient safety initiative.

Sincerely,



Nirav R. Shah, M.D., M.P.H.  
Commissioner of Health



James C. Cox  
Medicaid Inspector General

Attachments

**F329**

*Rev. 9-20-06.*

**§483.25(l) Unnecessary Drugs**

**1. General.** Each resident's drug regimen must be free from unnecessary drugs. An unnecessary drug is any drug when used:

- (i) In excessive dose (including duplicate therapy); or**
- (ii) For excessive duration; or**
- (iii) Without adequate monitoring; or**
- (iv) Without adequate indications for its use; or**
- (v) In the presence of adverse consequences which indicate the dose should be reduced or discontinued; or**
- (vi) Any combinations of the reasons above.**

**2. Antipsychotic Drugs.** Based on a comprehensive assessment of a resident, the facility must ensure that:

- (i) Residents who have not used antipsychotic drugs are not given these drugs unless antipsychotic drug therapy is necessary to treat a specific condition as diagnosed and documented in the clinical record; and**
- (ii) Residents who use antipsychotic drugs receive gradual dose reductions, and behavioral interventions, unless clinically contraindicated, in an effort to discontinue these drugs.**

**INTENT: §483.25(l)**

*The intent of this requirement is that each resident's entire drug/medication regimen be managed and monitored to achieve the following goals:*

- The medication regimen helps promote or maintain the resident's highest practicable mental, physical, and psychosocial well-being, as identified by the resident and/or representative(s) in collaboration with the attending physician and facility staff;*
- Each resident receives only those medications, in doses and for the duration clinically indicated to treat the resident's assessed condition(s);*
- Non-pharmacological interventions (such as behavioral interventions) are considered and used when indicated, instead of, or in addition to, medication;*
- Clinically significant adverse consequences are minimized; and*
- The potential contribution of the medication regimen to an unanticipated decline or newly emerging or worsening symptom is recognized and evaluated, and the regimen is modified when appropriate.*

**NOTE:** *This guidance applies to all categories of medications including antipsychotic medications.*

*Although the regulatory language refers to “drugs,” the guidance in this document generally will refer to “medications,” except in those situations where the term “drug” has become part of an established pharmaceutical term (e.g., adverse drug event, and adverse drug reaction or consequence).*

*For purposes of this guidance, references to “the pharmacist” mean the facility’s licensed pharmacist, whether employed directly by the facility or through arrangement.*

*The surveyor’s review of medication use is not intended to constitute the practice of medicine. However, surveyors are expected to investigate the basis for decisions and interventions affecting residents.*

## **DEFINITIONS**

*Definitions are provided to clarify terminology related to medications and to the evaluation and treatment of residents.*

- *“Adverse consequence” is an unpleasant symptom or event that is due to or associated with a medication, such as impairment or decline in an individual’s mental or physical condition or functional or psychosocial status. It may include various types of adverse drug reactions and interactions (e.g., medication-medication, medication-food, and medication-disease).*

**NOTE:** *Adverse drug reaction (ADR) is a form of adverse consequences. It may be either a secondary effect of a medication that is usually undesirable and different from the therapeutic effect of the medication or any response to a medication that is noxious and unintended and occurs in doses for prophylaxis, diagnosis, or treatment. The term “side effect” is often used interchangeably with ADR; however, side effects are but one of five ADR categories, the others being hypersensitivity, idiosyncratic response, toxic reactions, and adverse medication interactions. A side effect is an expected, well-known reaction that occurs with a predictable frequency and may or may not constitute an adverse consequence.*

- *“Anticholinergic side effect” is an effect of a medication that opposes or inhibits the activity of the parasympathetic (cholinergic) nervous system to the point of causing symptoms such as dry mouth, blurred vision, tachycardia, urinary retention, constipation, confusion, delirium, or hallucinations.*

- *“Behavioral interventions” are individualized non-pharmacological approaches (including direct care and activities) that are provided as part of a supportive physical and psychosocial environment, and are directed toward preventing, relieving, and/or accommodating a resident’s distressed behavior.*
- *“Clinically significant” refers to effects, results, or consequences that materially affect or are likely to affect an individual’s mental, physical, or psychosocial wellbeing either positively by preventing, stabilizing, or improving a condition or reducing a risk, or negatively by exacerbating, causing, or contributing to a symptom, illness, or decline in status.*
- *“Distressed behavior” is behavior that reflects individual discomfort or emotional strain. It may present as crying, apathetic or withdrawn behavior, or as verbal or physical actions such as: pacing, cursing, hitting, kicking, pushing, scratching, tearing things, or grabbing others.*
- *“Dose” is the total amount/strength/concentration of a medication given at one time or over a period of time. The individual dose is the amount/strength/concentration received at each administration. The amount received over a 24-hour period may be referred to as the daily dose.*
  - *“Excessive dose” means the total amount of any medication (including duplicate therapy) given at one time or over a period of time that is greater than the amount recommended by the manufacturer’s label, package insert, current standards of practice for a resident’s age and condition, or clinical studies or evidence-based review articles that are published in medical and/or pharmacy journals and that lacks evidence of:*
    - *A review for the continued necessity of the dose;*
    - *Attempts at, or consideration of the possibility of, tapering a medication; and*
    - *A documented clinical rationale for the benefit of, or necessity for, the dose or for the use of multiple medications from the same pharmacological class.*
- *“Duplicate therapy” refers to multiple medications of the same pharmacological class/category or any medication therapy that substantially duplicates a particular effect of another medication that the individual is taking.*
- *“Duration” is the total length of time the medication is being received.*
  - *“Excessive Duration” means the medication is administered beyond the manufacturer’s recommended time frames or facility-established stop order policies, beyond the length of time advised by current standards of practice, clinical practice guidelines, clinical studies or evidence-based review articles, and/or without either evidence of additional therapeutic*

*benefit for the resident or clinical evidence that would warrant the continued use of the medication.*

- *“Extrapyramidal symptoms (EPS)” are neurological side effects that can occur at any time from the first few days of treatment to years later. EPS includes various syndromes such as:*
  - *Akathisia, which refers to a distressing feeling of internal restlessness that may appear as constant motion, the inability to sit still, fidgeting, pacing, or rocking.*
  - *Medication-induced Parkinsonism, which refers to a syndrome of Parkinson-like symptoms including tremors, shuffling gait, slowness of movement, expressionless face, drooling, postural unsteadiness and rigidity of muscles in the limbs, neck and trunk.*
  - *Dystonia, which refers to an acute, painful, spastic contraction of muscle groups (commonly the neck, eyes and trunk) that often occurs soon after initiating treatment and is more common in younger individuals.*
- *“Gradual Dose Reduction (GDR)” is the stepwise tapering of a dose to determine if symptoms, conditions, or risks can be managed by a lower dose or if the dose or medication can be discontinued.*
- *“Indications for use” is the identified, documented clinical rationale for administering a medication that is based upon an assessment of the resident’s condition and therapeutic goals and is consistent with manufacturer’s recommendations and/or clinical practice guidelines, clinical standards of practice, medication references, clinical studies or evidence-based review articles that are published in medical and/or pharmacy journals.*
- *“Insomnia” is the inability to sleep characterized by difficulty falling asleep, difficulty staying asleep, early waking, or non-restorative sleep, which may result in impaired physical, social, or cognitive function.*
- *“Medication Interaction” is the impact of another substance (such as another medication, nutritional supplement including herbal products, food, or substances used in diagnostic studies) upon a medication. The interactions may alter absorption, distribution, metabolism, or elimination. These interactions may decrease the effectiveness of the medication or increase the potential for adverse consequences.*
- *“Medication Regimen Review” (MRR) is a thorough evaluation of the medication regimen by a pharmacist, with the goal of promoting positive outcomes and minimizing adverse consequences associated with medication. The review includes preventing, identifying, reporting, and resolving medication-related*

*problems, medication errors, or other irregularities in collaboration with other members of the interdisciplinary team.1*

- *“Monitoring” is the ongoing collection and analysis of information (such as observations and diagnostic test results) and comparison to baseline data in order to:*
  - *Ascertain the individual’s response to treatment and care, including progress or lack of progress toward a therapeutic goal;*
  - *Detect any complications or adverse consequences of the condition or of the treatments; and*
  - *Support decisions about modifying, discontinuing, or continuing any interventions.*
- *“Neuroleptic Malignant Syndrome” (NMS) is a syndrome related to the use of medications, mainly antipsychotics, that typically presents with a sudden onset of diffuse muscle rigidity, high fever, labile blood pressure, tremor, and notable cognitive dysfunction. It is potentially fatal if not treated immediately, including stopping the offending medications.*
- *“Non-pharmacological interventions” refers to approaches to care that do not involve medications, generally directed towards stabilizing or improving a resident’s mental, physical or psychosocial well-being.*
- *“Psychopharmacological medication” is any medication used for managing behavior, stabilizing mood, or treating psychiatric disorders.*
- *“Serotonin Syndrome” is a potentially serious clinical condition resulting from overstimulation of serotonin receptors. It is commonly related to the use of multiple serotonin-stimulating medications (e.g., SSRIs, SNRIs, triptans, certain antibiotics). Symptoms may include restlessness, hallucinations, confusion, loss of coordination, fast heart beat, rapid changes in blood pressure, increased body temperature, overactive reflexes, nausea, vomiting and diarrhea.*
- *“Tardive dyskinesia” refers to abnormal, recurrent, involuntary movements that may be irreversible and typically present as lateral movements of the tongue or jaw, tongue thrusting, chewing, frequent blinking, brow arching, grimacing, and lip smacking, although the trunk or other parts of the body may also be affected.*



Suggested Protocol for Prescribing Antipsychotic Drugs to the Elderly, to promote compliance with 42 CFR 483.25 F329, Unnecessary Medications:

1. Whenever a resident is admitted on an antipsychotic medication, or an antipsychotic medication is added to a resident's regimen, the attending physician must document the medical necessity for the medication by identifying the target symptoms/behaviors, and the diagnosis applicable to the medication chosen.
2. If usage of this medication is "off-label" and/or in contravention of "black box" FDA warning, attending physician or other prescriber must document the benefits to be achieved by the medication and the benefit/risk analysis.
3. Attending physician must document efforts undertaken to work up patient regarding target behaviors/symptoms: ruling out of infection (UTI, URI, etc.), head injury or other trauma, psychological and/or social upset, etc.
4. Attending physician must document the explanation of the benefit/risk analysis given when informed consent was obtained from patient or healthcare proxy/POA.
5. Documentation should include when the medication is to be initiated, the dose (and if it is not the lowest dose, the rationale for a higher dose), anticipated response; a gradual dose reduction plan; a discontinuation plan or documentation supporting continued use of the medication and the dosage and duration at which it will be continued.
6. Document specific plan for behavioral assessment and interventions to address target symptoms/behaviors.
7. Facility should have policy which addresses the need for the consultant pharmacist to review the medication regimen within 48 hours (not currently required per CFR; see Attachment 3 from CMS Partnership).
8. Facility's policies and procedures should include reference to applicable clinical practice guidelines (see Attachment #5, p.7 as example).
9. Document in patient's clinical record response (or lack thereof) to medication, and any adverse effects; monitoring should be documented by nursing, physicians, pharmacist, and any psychologist, psychiatrist, Social Worker or other mental health professional involved with care of patient. Medication Regimen Review should be documented by attending physician and pharmacist on regular schedule (monthly at a minimum).

**PARTNERSHIP TO IMPROVE DEMENTIA CARE  
IN NURSING HOMES**

**\*Questions to Consider in  
Interdisciplinary Team Review of  
Individual Dementia Care Cases**

- If the behavioral symptoms represent a change or worsening, was a medical work up performed to rule out underlying medical or physical causes of the behaviors, if appropriate?
- Were current medications considered as potential causes of the behaviors (i.e., those with significant anticholinergic or other side effects)?
- If a medical cause (e.g., UTI) was identified, was treatment (if indicated) initiated in a timely manner?
- If medical causes were ruled out, did the staff attempt to establish the root causes of the behaviors, using a careful and systematic process and individualized knowledge about the resident when possible? Were family caregivers or others who knew the resident prior to his/her dementia consulted about prior life patterns, responses to stress, etc.?
- Was the initial clinical indication for the medication valid?
- Were non-pharmacologic, person-centered interventions tried before medications (other than in an emergency)? Were the results documented?

- Were specific target behaviors identified and desired outcomes related to those behaviors documented? Were caregivers aware of the target behaviors and desired results of the medication?
- Was the resident or appropriate legal representative consulted about the decision to use an antipsychotic medication and was that discussion documented?
- If a drug is continued for more than a few weeks, is the original clinical indication still valid (are the behaviors still present)?
- Is appropriate monitoring in place and is the team aware of the potential side effects?
- If new symptoms or changes in condition occurred after an antipsychotic medication was started, was medication use considered as a potential cause of a change or symptom?
- If on a medication, did the pharmacist perform a medication regimen review and identify related signs and symptoms, or did the staff inform the pharmacist if symptoms occurred after the last pharmacist visit?

## Partnership to Improve Dementia Care in Nursing Homes Suggestions for Provider Checklist

% of residents in facility on atypical antipsychotics: \_\_\_\_\_ Quality Measure State Percentile Rank – antipsychotics: \_\_\_\_\_

|  | YES | NO |
|--|-----|----|
| Staff in all departments, are trained in person-centered care and how to respond effectively to behaviors (access sample training programs on Advancing Excellence website; Hand in Hand).   |     |    |
| In addition to medical and psychiatric history, recent changes in behavior or cognition and other standard clinical evaluations, at admission information is obtained from the resident, family, and/or caregivers on the resident's preferences, routines, pre-dementia personality, social patterns, responses to stress and effective interventions.  |     |    |
| The information obtained on during the admission process is conveyed to direct caregivers.   |     |    |
| This admission information is integrated into the care plan and may be revised over time as the resident's condition and needs change.   |     |    |
| Interviews with staff demonstrate that they have implemented and are following the care plan, continue to seek input from family members or care givers for unresolved issues, and communicate with practitioners regarding change in condition or new or persistent symptoms.   |     |    |
| If a resident is placed on an antipsychotic medication, there is documentation in the record that the resident or appropriate legal representative was involved in the decision.   |     |    |
| Facility has consistent staff assignments (same Certified Nursing Assistant to same resident 5 days/week).   |     |    |
| Certified Nursing Assistant to Resident Ratio 1 <sup>st</sup> shift/2 <sup>nd</sup> shift/3 <sup>rd</sup> shift  |     |    |
| Senior leadership (Nursing Home Administrator, Director of Nursing, Medical Director) attend care plan meetings periodically for residents with unresolved behavioral or psychological symptoms of dementia.   |     |    |
| Interdisciplinary team seeks input at care plan meetings from the Medical Director, Consultant Pharmacist and Certified Nursing Assistants for residents with behavioral or psychological symptoms.  |     |    |
| Providers conduct outreach and education to the resident's family and strongly encourage their participation in care plan meetings (offering to flex the schedule or use conference calls when the family cannot physically be in attendance).   |     |    |
| Nursing Home Administrators and Directors of Nursing review quality measures (e.g., monthly) and use the Quality Measures report to identify residents who may need alternative interventions and oversee their implementation.  |     |    |
| Each month, Nursing Home Administrators and Directors of Nursing review Quality Measures report, along with the Pharmacy Consultant report, to identify residents appropriate for possible reduction/elimination of antipsychotics. The review of aggregate data should be combined with real-time, case-based information and input from practitioners. |     |    |
| Nursing Home Administrators and Directors of Nursing review Pharmacy Consultant's report quarterly with Consultant Pharmacist and Medical Director to track and trend data.  |     |    |
| Direct caregivers (Certified Nursing Assistants), together with the family and care plan team, is involved in the process of developing and implementing effective, person-specific interventions to address behavioral symptoms.  |     |    |
| If any resident is admitted on an antipsychotic or is started on an antipsychotic after admission, the Consultant Pharmacist, along with the practitioner, reviews that resident's care plan, including all medications, within 24-48 hours.   |     |    |
| A documented process is in place and is utilized when initiating an antipsychotic prescription (e.g., standard order set, decision support algorithm, routine monitoring recommendations, etc.).   |     |    |

**"Yes" answers require supporting documentation and visual confirmation by quality improvement personnel.**



## CMS Partnership to Improve Dementia Care in Nursing Homes

### RESOURCES

*Updated 6/28/2012*

#### CMS Launches Partnership to Improve Dementia Care in Nursing Homes

On March 29, via a video streaming event, CMS launched a new initiative aimed at improving behavioral health and safeguarding nursing home residents from unnecessary antipsychotic drug use. As part of the initiative, CMS is developing a national action plan that will use a multidimensional approach including public reporting, raising public awareness, regulatory oversight, technical assistance/training and research. The action plan will be targeted at enhancing person-centered care for nursing home residents, particularly those with dementia-related behaviors. [Watch the CMS video.](#)

#### **CMS' Partnership to Improve Dementia Care in Nursing Homes:**

[Clive Ballard's Presentation on Management of Behavioral and Psychological Symptoms in People with Dementia Living in Care Homes: A UK Perspective](#)

*From Dr. Peter Rabins:*

[Assessment Form for Residents with Dementia](#)

#### Additional Resources from Advancing Excellence Partners

##### **Alzheimer's Association**

*Massachusetts/New Hampshire Chapter*

*From Dr. Paul Raia:*

[Sleuthing Troublesome Behaviors](#)

[Habilitation Therapy: A New Starscape](#)

[http://www.alz.org/professionals\\_and\\_researchers\\_dementia\\_care\\_practice\\_recommendations.asp](http://www.alz.org/professionals_and_researchers_dementia_care_practice_recommendations.asp)

Contact:

Cyndy Cordell

[cyndy.cordell@alz.org](mailto:cyndy.cordell@alz.org)

##### **The American Geriatrics Society (AGS)**

<http://www.americangeriatrics.org>

**American Health Care Association (AHCA)**

[http://www.ahcanca.org/QUALITY\\_IMPROVEMENT/QUALITYINITIATIVE/Pages/default.aspx](http://www.ahcanca.org/QUALITY_IMPROVEMENT/QUALITYINITIATIVE/Pages/default.aspx)

Contact:

Sandy Fitzler

[sfitzler@AHCA.org](mailto:sfitzler@AHCA.org)

202-898-6307

**American Medical Directors Association (AMDA)**

Psychopharmacologic Interdisciplinary Medication Review

Sample Psychotropic Medication Policy

Contact:

Karyn Leible

[kleible@jewishseniorlife.org](mailto:kleible@jewishseniorlife.org)

585-784-6405

*AMDA's Clinical Practice Guidelines*

Dedicated to Long Term Care Medicine: Excerpt from AMDA Dementia Clinical Practice Guideline

<http://www.amda.com/advocacy/brucbs.cfm>

**American Society of Consultant Pharmacists**

<http://www.ascp.com/antipsychotic>

Contact:

Arnold Clayman

[aclayman@ascp.com](mailto:aclayman@ascp.com)

703-739-1300

**California Advocates for Nursing Home Reform (CANHR)**

[http://www.canhr.org/stop\\_drugging](http://www.canhr.org/stop_drugging)

Contact:

Michael Conners

[Michael@canhr.org](mailto:Michael@canhr.org)

Contact:

Anthony Chicotel

[tony@canhr.org](mailto:tony@canhr.org)

**The Consumer Voice**

*Long Term Care Ombudsmen Resource Center Issue Overview*

<http://www.theconsumervoic.org/advocate/antipsychotic-drugs>

*Fact Sheet including guidance to residents and advocates regarding individualized assessment where an individual has behavioral symptoms*

[http://www.theconsumervoic.org/sites/default/files/advocate/advocacy-groups/INDIVIDUALIZED\\_ASSESSMENT with Behavior Symptoms.pdf](http://www.theconsumervoic.org/sites/default/files/advocate/advocacy-groups/INDIVIDUALIZED_ASSESSMENT_with_Behavior_Symptoms.pdf)

Contact:

Janet Wells

[jwells@theconsumervoice.org](mailto:jwells@theconsumervoice.org)

*Person-centered Care Planning*

<http://www.theconsumervoice.org/sites/default/files/resident/nursing-home/assessment-and-care-planning.pdf>

#### **Department of Veterans Affairs**

<http://www.ncbi.nlm.nih.gov/books/NBK54971>

#### **The Eden Alternative**

*The Eden Alternative has created a webpage that summarizes new groundbreaking educational offerings designed to introduce providers to fundamental and advanced techniques in person-directed care proven to reduce the off-label use of antipsychotic drugs.*

<http://www.edenalt.org/how-we-serve/reduce-the-use-of-antipsychotic-medications-in-people-living-in-long-term-care-settings>

Contact:

Meredith Burrus

Education Coordinator

The Eden Alternative

(615) 785-1600

(585) 461-3951

[education@edenalt.org](mailto:education@edenalt.org)

#### **LeadingAge**

<http://www.leadingage.org/Newsletter.aspx?id=4694&pv=t>

Contact:

Cheryl Phillips, M.D.

[cphillips@leadingage.org](mailto:cphillips@leadingage.org)

#### **National Gerontological Nursing Association (NGNA)**

<http://www.ngna.org>

#### **The National Long-Term Care Ombudsman Resource Center**

*Person-centered Care Planning*

[http://www.ltombudsman.org/ombudsman-support/training#Training\\_Programs\\_and\\_In-services](http://www.ltombudsman.org/ombudsman-support/training#Training_Programs_and_In-services)

#### **Quality Improvement Organizations**

*Alliant | GMCF*

[Reducing Inappropriate Use of Antipsychotics in Nursing Homes - part 1](#)

[Reducing Inappropriate Use of Antipsychotics in Nursing Homes - part 2](#)



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**Sent:** Friday, July 20, 2012 12:30 PM

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**Cc:** Laughman, Michele L. (CMS/OCSQ)

**Subject:** Partnership to Improve Dementia Care in Nursing Homes -- New York Follow-Up (Revised Contact List)

Good Afternoon,

Thank you for participating in the recent State call for the *Partnership to Improve Dementia Care in Nursing Homes*.

I wanted to share some information I obtained after our call. I have learned that if a state is interested in obtaining additional funds for their Coalition, through the use of CMP funds, they can submit a project proposal to their State Agency. Some of the Regional Offices, such as RO-IV, have CMP Grant Applications as well. (S&C 12-13 Use of CMP Funds by States) Attached you will find this information.

**Suggested Next Steps:**

Your State Coalition should become familiar with the guidance at F329.

Accessing web sites, such as Advancing Excellence, researching professional organizations and/or utilizing the services of consultants are all great ways to find helpful resources/tools that already exist.

CMS can share some tools/resources which are currently under development to assist your State Coalition in completing provider outreach, including:

- o Provider Question Worksheet
- o Flow Diagram for Providers
- o Performance Indicator Checklist

- Example AMDA Letter (attached)  
(The additional above listed tools/resources will be provided as soon as they have been finalized and approved for distribution.)

Communicate with the physicians who practice and prescribe for this elderly population in your State.

Communicate with the providers in your area, collaborating on reinforcing the individualized approach to resident care that involves meeting their true needs. Communicate your support to the providers, state agency and surveyors in approaches and methods that you have experience and found to be successful.

Involve the residents and their families as the first hand stakeholders that they are.

Develop guidance on how nursing homes will take the first steps toward analyzing their own data – make sure homes know how they can get their data, changes to the measures coming soon, how they will mobilize their leadership team (DON, administrator, medical director, pharmacist), how they will review all residents on antipsychotics monthly (or as needed) and how they will begin GDRs on appropriate residents.

#### **Suggested Goals:**

**One Month Goal** – Review Nursing Home Compare and identify which facilities have a high rate of antipsychotic drug use; Target these facilities and provide outreach

**Three Month Goal** – Provide direction to target facilities related to CMS Initiative, including Provider Worksheet and resources/tools

**Six Month Goal** – Obtain consistent feedback from target facilities related to progress towards National Goal- December 2012 is deadline for 15% reduction; Report findings to CMS

Progress and success toward your goals can be, in part, monitored through the new Quality Measures that are being established and that will be posted on the Nursing Home Quality webpage starting in July 2012. In the meantime, you can begin to assess the data that is currently there, establishing a starting point to be used as a metric of measurement.

#### **Questions:**

- Consumers may be directed to the Advancing Excellence homepage at [www.nhqualitycampaign.org](http://www.nhqualitycampaign.org)
- Surveyors may be directed to the Kick-Off webinar at [www.youtube.com/watch?v=U1\\_rpO0bwbM](http://www.youtube.com/watch?v=U1_rpO0bwbM)
- General questions may be sent to the Core Team for this initiative via [dnh\\_behavioralhealth@cms.hhs.gov](mailto:dnh_behavioralhealth@cms.hhs.gov)

I hope you find this information to be helpful. If you have any questions or concerns, please feel free to contact me.

Thank you,

Michele

*Michele Laughman*

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# Management of Alzheimer's Disease and Related Dementias

## Guidelines Being Compared:

1. **American College of Physicians/American Academy of Family Physicians (ACP/AAFP)**. Current pharmacologic treatment of dementia: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med* 2008 Mar 4;148(5):370-8. [63 references]
2. **American Psychiatric Association (APA)**. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias. Arlington (VA): American Psychiatric Association (APA); 2007 Oct. 85 p. [554 references]
3. **National Institute for Health and Clinical Excellence (NICE)**. Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Mar. 84 p. (Technology appraisal guidance; no. 217)
4. **Singapore Ministry of Health (SMOH)**. Dementia. Singapore: Singapore Ministry of Health; 2007 Mar. 80 p. [162 references]

A direct comparison of recommendations presented in the above guidelines for the management of Alzheimer's disease (AD) and related dementias is provided below.

## Areas of Agreement

### Pharmacological Management of Dementia

Three groups—APA, NICE, and SMOH—provide explicit recommendations regarding appropriate medications for a certain type and/or severity of dementia. The guideline developers agree that the three cholinesterase inhibitors donepezil, rivastigmine and galantamine are the primary medications used in the management of

AD, and should be considered for the management of patients with **mild to moderate** disease. There is less agreement regarding their use in **severe** AD—refer to Areas of Difference below for information.

With regard to the use of cholinesterase inhibitors for types of dementia other than AD, APA and SMOH agree that they can be considered for patients with dementia with Lewy bodies and dementia associated with Parkinson's disease. APA specifies that only rivastigmine has been approved by the FDA for the latter indication, but that there is no reason to believe the benefit is specific to this cholinesterase inhibitor. NICE did not assess the benefits of cholinesterase inhibitors for patients with forms of dementia other than AD.

There is consensus that the NMDA antagonist memantine can be considered for the management of **moderate** and **severe** AD (NICE specifies that use in people with moderate disease should be reserved for those who are intolerant of or have a contraindication to cholinesterase inhibitors). There is less agreement regarding its use in **mild** AD—refer to Areas of Difference below for information.

ACP/AAFP does not provide recommendations for the use of particular pharmacological agents, but rather recommends clinicians base this choice on tolerability, adverse effect profile, ease of use, and cost of medication. They add that the evidence is insufficient to compare the effectiveness of different pharmacologic agents for the treatment of dementia. The ACP/AAFP guideline focuses primarily on prescribing practices, more specifically the decision to initiate pharmacologic therapy, factors to consider in choosing a pharmacological agent, and research needed on the clinical effectiveness of pharmacologic management of dementia.

NICE specifies that pharmacological treatment be initiated only by specialists in the care of patients with dementia; that patients who continue treatment should be reviewed regularly using cognitive, global, functional, and behavioral assessment; and that carers' views on the patient's condition should be sought at baseline and at follow-up. NICE also cites circumstances in which it is inappropriate to rely solely on the patient's cognition scores when assessing the severity of AD and the need for treatment. In such cases, they recommend healthcare professionals use another appropriate method of assessment.

#### **Other Pharmacologic Agents**

APA and SMOH agree that other classes of medication may be appropriate for the treatment of dementia-related symptoms including depression, psychosis, and anxiety. The groups agree that antidepressants may be used for the treatment of comorbid depression, provided their use has been evaluated carefully for each patient, and that the antidepressant trazodone may be appropriate for patients with dementia-associated agitation. The guidelines agree that, if necessary, antipsychotics may be recommended with caution, given their side effect profile, to treat the neuropsychiatric symptoms of dementia.

APA and SMOH further agree that the available effectiveness and safety data for other agents, including vitamin E, Ginkgo biloba, hydroxychloroquine, prednisolone, statin medications, selegiline, estrogen and NSAIDs, do not support recommendations for the treatment of core or associated symptoms in people with

AD at this time. There is also agreement that anticonvulsants (e.g., sodium valproate) and mood stabilizers (e.g., lithium) are not indicated for routine use in the management of AD and its associated symptoms.

The NICE technology appraisal only addresses donepezil, galantamine, rivastigmine and memantine.

#### **Patient and Caregiver Education**

APA emphasizes the importance of communicating with the patient (as appropriate) and caregivers regarding the patient's status, treatment plan, and approaches to behavioral management. APA also underscores the need for the physician to be familiar with and make referrals to community support services, such as adult day care programs and AD support organizations.

## Areas of Difference

#### **Cholinesterase Inhibitors for the Management of Severe AD**

While NICE recommends cholinesterase inhibitors as options for managing AD of **mild to moderate** severity only, SMOH states that they can be considered for the management of **moderate to severe** AD. APA similarly states that cholinesterase inhibitors may be helpful for patients with **severe** AD.

#### **Memantine for the Management of Mild AD**

NICE recommends memantine as an option only for managing **moderate** AD (in people who are intolerant of or have a contraindication to cholinesterase inhibitors) and **severe** AD. SMOH, in contrast, deems it an option for the management of **mild to moderate** AD if cholinesterase inhibitor therapy is contraindicated, not tolerated, or if there is disease progression despite an adequate trial of a cholinesterase inhibitor. APA notes that there is some evidence of memantine's benefit in mild AD, but the developer does not make an explicit recommendation for its use for this level of severity.

#### **Cholinesterase Inhibitors for the Management of Vascular Dementia**

SMOH states that cholinesterase inhibitors have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia. APA, in contrast, states that the constructs of mild cognitive impairment and vascular dementia are evolving and have ambiguous boundaries with AD. The efficacy and safety of cholinesterase inhibitors for patients with these disorders are uncertain, APA continues, and therefore makes no specific recommendation, noting that individual patients may benefit from these agents.

NICE did not assess the benefits of the three cholinesterase inhibitors for patients with forms of dementia other than AD.

#### **Memantine for the Management of Vascular Dementia**

While APA and SMOH agree on the use of memantine for AD, there is less agreement regarding its efficacy in the management of vascular dementia. According to APA, there is very limited evidence of its benefit in vascular dementia. SMOH, in contrast, provides a grade "A" recommendation, stating that NMDA antagonists have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia. ACP/AAFP notes that patients with mild vascular dementia have shown mild benefit from memantine. They add, however, that memantine use in mild AD has not been well studied.

## General Management Recommendations

|                                   |  |
|-----------------------------------|--|
| <p><b>ACP/AAFP<br/>(2008)</b></p> | <p>No recommendations offered.</p>   |
| <p><b>APA<br/>(2007)</b></p>      | <p><b><u>General Treatment Principles and Alternatives</u></b></p> <p>Patients with dementia display a broad range of cognitive impairments and neuropsychiatric symptoms that can cause significant distress to themselves and caregivers. As a result, individualized and multimodal treatment plans are required [I]. Dementia is usually progressive, and treatment must evolve with time in order to address newly emerging issues [I]. At each stage the psychiatrist should be vigilant for symptoms likely to be present, should identify and treat co-occurring psychiatric and medical conditions, and should help patients and families anticipate future symptoms and the care likely to be required [I].</p> <p><b>Psychiatric Management</b></p> <p>The treatment of patients with dementia should be based on a thorough psychiatric, neurological, and general medical evaluation of the nature and cause of the cognitive deficits and associated noncognitive symptoms, in the context of a solid alliance with the patient and family [I]. It is particularly critical to identify and treat general medical conditions, most notably delirium, that may be responsible for or contribute to the dementia or associated neuropsychiatric symptoms [I].</p> <p>Ongoing assessment includes periodic monitoring of the development and evolution of cognitive and noncognitive psychiatric symptoms and their response to intervention [I]. In order to offer prompt treatment, enhance safety, and provide timely advice to the patient and family, it is generally necessary to see patients in routine follow-up at least every 3 to 6 months [II]. More frequent visits (e.g., up to once or twice a week) or even psychiatric hospitalization may be required for patients with acute, complex, or potentially dangerous symptoms or for the administration of specific therapies [I]. Recommended assessments include evaluation of suicidality, dangerousness to self and others, and the potential for aggression, as well as evaluation of living conditions, safety of the environment, adequacy of</p> |

|                    |  |
|--------------------|--|
|                    | <p>supervision, and evidence of neglect or abuse <b>[I]</b>.</p> <p>All patients and families should be informed that even mild dementia increases the risk of vehicular accidents <b>[I]</b>. Mildly impaired patients should be advised to limit their driving to safer situations or to stop driving <b>[I]</b>, and moderately impaired patients should be instructed not to drive <b>[I]</b>. Advice about driving cessation should also be communicated to family members, as the implementation of the recommendation often falls on them <b>[I]</b>. Relevant state laws regarding notification should be followed <b>[I]</b>.</p> |
| <b>NICE (2011)</b> | No recommendations offered.  |
| <b>SMOH (2007)</b> | <p><b>Social and Caregiver Management of Dementia and Community Resources</b></p> <p><b>A</b> - Caregiver interventions via a multifaceted approach should be considered in the total management of the person with dementia. <b>(Grade A, Level 1+)</b></p> <p><b>GPP</b> - Where appropriate, respite care can be offered to relieve the burden of caregiving on the family caregiver.</p> <p><b>GPP</b> - Referral to community resources to meet the care needs of the person with dementia and his/her carer should always be considered.</p>   |

### Non-pharmacologic Interventions (Back to top)

|                        |   |
|------------------------|---|
| <b>ACP/AAFP (2008)</b> | No recommendations offered.   |
| <b>APA (2007)</b>      | <p><b>Specific Psychotherapies and Other Psychosocial Treatments</b></p> <p>In addition to the general psychosocial interventions subsumed under psychiatric management, a number of specific interventions are appropriate for some patients. Few of these treatments have been subjected to double-blind randomized evaluation, but some research, along with clinical practice, supports their effectiveness. Behavior-oriented treatments are used to identify the antecedents and consequences of problem behaviors and attempt to reduce the frequency of behaviors by directing changes in the environment that alter these antecedents and consequences. Behavioral approaches have not been subjected to large randomized clinical trials but are supported by small trials and case studies and are</p> |

in widespread clinical use [II]. Stimulation-oriented treatments, such as recreational activity, art therapy, music therapy, and pet therapy, along with other formal and informal means of maximizing pleasurable activities for patients, have modest support from clinical trials for improving behavior, mood, and, to a lesser extent, function, and common sense supports their use as part of the humane care of patients [II]. Among the emotion-oriented treatments, supportive psychotherapy can be employed to address issues of loss in the early stages of dementia [II]. Reminiscence therapy has some modest research support for improvement of mood and behavior [III]; validation therapy and sensory integration have less research support [III]; none of these modalities has been subjected to rigorous testing. Cognition-oriented treatments, such as reality orientation, cognitive retraining, and skills training focused on specific cognitive deficits, are unlikely to have a persistent benefit and have been associated with frustration in some patients [III].

#### **Treatment of Psychosis and Agitation**

Psychosis, aggression, and agitation are common in patients with dementia and may respond to similar therapies. When deciding if treatment is indicated, it is critical to consider the safety of the patient and those around him or her [I]. A careful evaluation for general medical, psychiatric, environmental, or psychosocial problems that may underlie the disturbance should be undertaken [I]. If possible and safe, such underlying causes should be treated first [I]. If this does not resolve the symptoms, and if they do not cause significant danger or distress to the patient or others, such symptoms are best treated with environmental measures, including reassurance and redirection [I]. For agitation, some of the behavioral measures discussed in Item 2 above may also be helpful [II]. If these measures are unsuccessful or the behaviors are particularly dangerous or distressing, then the symptoms may be treated judiciously with one of the agents discussed in the following paragraphs [II]. The use of such agents should be reevaluated and their benefit documented on an ongoing basis [I].

#### **Treatment of Depression**

Depression is common in patients with dementia. Patients with depression should be evaluated for suicide risk [I]. Depressed mood may respond to improvements in the patient's living situation or to stimulation-oriented treatments [II].

#### **Treatment of Sleep Disturbances**

Sleep disturbances are common in patients with dementia. Interventions include maintaining daytime activities and giving careful attention to sleep hygiene [II]. Pharmacological intervention could be considered when other approaches have failed [II].

### Special Issues for Long-Term Care

Many patients eventually require long-term-care placement; approximately two-thirds of nursing home patients have dementia. Care should be organized to meet the needs of patients, including those with behavioral problems [I]. Employing staff with knowledge and experience concerning dementia and the management of difficult behavior is important [II]. Special care units may offer more optimal care, although there is limited evidence that they achieve better outcomes than traditional units [III].

A particular concern is the use of physical restraints and medications to control disruptive behavior.

Appropriate use of antipsychotic medications can relieve symptoms and reduce distress and can increase safety for patients, other residents, and staff [I]. However, their use may be associated with worsening cognitive impairment, oversedation, falls, tardive dyskinesia, and neuroleptic malignant syndrome, as well as with hyperlipidemia, weight gain, diabetes mellitus, cerebrovascular accidents, and death [I]. Thus, good clinical practice requires careful consideration and documentation of the indications and available alternatives, both initially and on a regular ongoing basis [I]. A dose decrease or discontinuation should be considered periodically for all patients who receive antipsychotic medications [I]. A structured education program for staff may help to both manage patients' behavior and decrease the use of these medications in nursing homes [II].

Physical restraints are rarely indicated and should be used only for patients who pose an imminent risk of physical harm to themselves or others [I]. Reasons for the use of physical restraints should be carefully documented [I]. The need for restraints can be decreased by environmental changes that decrease the risk of falls or wandering and by careful assessment and treatment of possible causes of agitation [II].

**NICE  
(2011)**

No recommendations offered.

**SMOH  
(2007)**

#### **Management of Behavioural and Psychological Symptoms of Dementia (BPSD)**

**GPP** - Non-pharmacological methods to manage behavioural and psychological symptoms of dementia should be instituted, prior to consideration of pharmacological measures.

## Pharmacologic Interventions

ACP/AAFP  
(2008)

**Recommendation 1:** *Clinicians should base the decision to initiate a trial of therapy with a cholinesterase inhibitor or memantine on individualized assessment. (Grade: weak recommendation, moderate-quality evidence.)*

The decision to initiate therapy should be based on evaluation of benefits and risks associated with an individual patient. In particular, in more advanced dementia, family or other decision makers may not view stabilization or slowing of decline as a desirable goal if quality of life is judged to be poor. All of the drugs have known adverse events, and the decision to manage patients with dementia should balance harms against modest or even no benefit. Although the evidence shows statistically significant benefits of treatment with some cholinesterase inhibitors and memantine for all kinds of dementia, these benefits, on average, are not clinically significant for cognition and are modest for global assessments. However, limited evidence suggests, but does not demonstrate conclusively, that a subgroup of patients achieves clinically important improvements. These findings should be interpreted cautiously because many trials did not report the proportion of patients who achieved clinically important improvements, and for trials that did, these outcomes were often not the primary end point of the trial. In addition, many trials that did report the proportion of patients who achieved clinically important improvements did not report the statistical significance of these findings. Currently, we have no way to predict which patients might have a clinically important response. Therefore, the evidence does not support prescribing these medications for every patient with dementia.

Evidence is insufficient to determine the optimal duration of therapy. A beneficial effect, if any, would generally be observed within 3 months on the basis of duration of trials. This effect could be an improvement or stabilization. In addition, no evidence demonstrates when it is appropriate to stop the treatment if the patient becomes unresponsive or shows decline in various domains of dementia. However, if slowing decline is no longer a goal, treatment with memantine or a cholinesterase inhibitor is no longer appropriate.

**Recommendation 2:** *Clinicians should base the choice of pharmacologic agents on tolerability, adverse effect profile, ease of use, and cost of medication. The evidence is insufficient to compare the effectiveness of different pharmacologic agents for the treatment of dementia. (Grade: weak recommendation, low-quality evidence.)*

Because few trials compare one drug with another, evidence about effectiveness is insufficient to support the choice of specific drugs for the treatment of dementia. Therefore, tolerability, adverse effect profile, ease of use, and cost of medication are reasonable criteria to help select a treatment. For example, when the benefits and harms related to a drug are being evaluated, the severe side effects associated with tacrine make it an unreasonable

choice.

Cholinesterase inhibitors discussed in this guideline are approved for treatment of mild to moderate dementia, and memantine is approved by the FDA for the treatment of moderate to severe AD. Patients with mild vascular dementia have shown mild benefit from memantine. However, memantine use in mild AD has not been well studied. Major contraindications of cholinesterase inhibitors and memantine include, but are not limited to, uncontrolled asthma, angle-closure glaucoma, the sick sinus syndrome, and left bundle-branch block.

**Recommendation 3:** *There is an urgent need for further research on the clinical effectiveness of pharmacologic management of dementia.*

Further research is needed to evaluate the effectiveness of pharmacologic therapy for dementia and to assess whether treatment affects outcomes, such as institutionalization. Evaluation of the appropriate duration of therapy and more head-to-head comparisons of agents are needed. Finally, assessment of the effectiveness of combination therapy is lacking.

**APA  
(2007)**

### **Special Concerns Regarding Somatic Treatments for Elderly Patients and Patients With Dementia**

Medications are effective in the management of some symptoms associated with dementia, but they must be used with caution in this patient population [I]. Because age may alter the absorption, distribution, metabolism, and elimination of many medications, elderly individuals may be more sensitive to their effects. General medical conditions and use of more than one medication may further affect the pharmacokinetics of many medications. In addition, patients with dementia may be more likely to experience certain medication adverse effects, including anticholinergic effects, orthostasis, sedation, and parkinsonism. Finally, symptoms of dementia may alter medication adherence in ways that are unsafe. Consequently, when using pharmacotherapy in patients with dementia, low starting doses, small increases in dose, and long intervals between dose increments may be needed, in addition to ensuring that a system is in place that can enhance proper medication adherence [I].

### **Treatment of Cognitive Symptoms**

Three cholinesterase inhibitors—donepezil, rivastigmine, and galantamine—are approved by the U.S. FDA for treatment of mild to moderate AD, and donepezil has been approved by the FDA for severe AD. These medications have similar rates of adverse effects and have been shown to lead to modest benefits in a substantial minority of patients (i.e., 30%-40% in clinical trials). These medications should be offered to patients with mild to moderate AD after a thorough discussion of their potential risks and benefits [I], and they may be helpful

for patients with severe AD [II].

Cholinesterase inhibitors should be considered for patients with mild to moderate dementia associated with Parkinson's disease [I]. Only rivastigmine has been approved by the FDA for this indication, but there is no reason to believe the benefit is specific to this cholinesterase inhibitor.

Cholinesterase inhibitors can be considered for patients with dementia with Lewy bodies [II].

The constructs of mild cognitive impairment and vascular dementia are evolving and have ambiguous boundaries with AD. The efficacy and safety of cholinesterase inhibitors for patients with these disorders are uncertain; therefore, no specific recommendation can be made at this time, although individual patients may benefit from these agents [II].

Memantine, a noncompetitive NMDA antagonist, which has been approved by the FDA for use in patients with moderate and severe AD, may provide modest benefits and has few adverse effects; thus, it may be considered for such patients [I]. There is some evidence of its benefit in mild AD [III] and very limited evidence of its benefit in vascular dementia [I].

Vitamin E (alpha-tocopherol) is no longer recommended for the treatment of cognitive symptoms of dementia because of limited evidence for its efficacy as well as safety concerns [II].

NSAIDs, statin medications, and estrogen supplementation (with conjugated equine estrogens) have shown a lack of efficacy and safety in placebo-controlled trials in patients with AD and therefore are not recommended [I].

#### **Treatment of Psychosis and Agitation**

On the basis of good evidence, antipsychotic medications are recommended for the treatment of psychosis in patients with dementia [II] and for the treatment of agitation [II]. These medications have also been shown to provide modest improvement in behavioral symptoms in general [I]. Evidence for the efficacy of these agents is based mostly on 6-12-week trials in nursing home residents and outpatients. There is limited research on their use beyond 12 weeks, but considerable clinical experience supports this practice [II]. Evidence for a difference in efficacy and safety among antipsychotic medications is limited. Antipsychotic medications as a group are associated with a number of severe adverse events, including increased risks for death, cerebrovascular accidents, tardive dyskinesia, neuroleptic malignant syndrome, hyperlipidemia, weight gain, diabetes mellitus, sedation, parkinsonism, and worsening of cognition. Thus, they must be used with caution and at the lowest effective dosage [I], after considering the risks of not treating the psychiatric symptoms [I]. Patients and families should be advised about potential benefits and risks of antipsychotic agents,

particularly the risk of mortality [I]. Second-generation (atypical) antipsychotics currently have a black box warning for increased risk of mortality in elderly patients; recent data suggest that first-generation (typical) agents carry at least a similar risk. High-potency agents tend to cause akathisia and parkinsonian symptoms; low-potency agents tend to cause sedation, confusion, delirium, postural hypotension, and peripheral anticholinergic effects. The decision of which antipsychotic to use is based on the relationship between the side-effect profile and the characteristics of the individual patient [I].

Data demonstrating benefit from benzodiazepines are modest, but benzodiazepines occasionally have a role in treating patients with prominent anxiety [III] or on an as-needed basis for patients with infrequent episodes of agitation or for those who require sedation for a procedure such as a tooth extraction or a diagnostic examination [II]. Adverse effects of benzodiazepines include sedation, worsening cognition, delirium, increased risk of falls, and worsening of breathing disorders. Lorazepam and oxazepam, which have no active metabolites, are preferable to agents with a longer half-life such as diazepam or clonazepam [III].

There is minimal evidence for the efficacy of anticonvulsants, lithium, and beta-blockers for the treatment of psychosis or agitation in dementia, and these medications have significant adverse effects; therefore, they are generally not recommended except for patients for whom other treatments have failed [III]. The antidepressant trazodone and the SSRIs are also not well studied for symptoms other than depression but may be appropriate for nonpsychotic patients with agitation, especially for patients with mild agitation or prior sensitivity to antipsychotic medications [III].

#### **Treatment of Depression**

Depression is common in patients with dementia. Patients with depression should be evaluated for suicide risk [I]. Depressed mood may respond to improvements in the patient's living situation or to stimulation-oriented treatments [II]. Although evidence for antidepressant efficacy in patients with dementia and depression is mixed, clinical consensus supports a trial of an antidepressant to treat clinically significant, persistent depressed mood [II]. The choice among agents is based on the side-effect profile of specific medications and the characteristics of the individual patient [I]. SSRIs may be preferred because they appear to be better tolerated than other antidepressants [II]. Bupropion, venlafaxine, and mirtazapine may also be effective [II]. Agents with substantial anticholinergic effects (e.g., amitriptyline, imipramine) should be avoided [I]. Despite the lack of research data, clinical experience suggests that unilateral electroconvulsive therapy (ECT) may be effective for patients who do not respond to pharmacological agents [II]:

Treatments for apathy are not well supported, but psychostimulants, bupropion, bromocriptine, and amantadine may be helpful [III]. Psychostimulants are also sometimes useful in the treatment of depression in patients with significant general medical illness [III].

#### **Treatment of Sleep Disturbances**

Pharmacological intervention could be considered when other approaches have failed [II]. If a patient also requires medication for another psychiatric condition, an agent with sedating properties, given at bedtime, could be selected [I]. For primarily treating the sleep disturbance, medications with possible effectiveness include trazodone, zolpidem, or zaleplon [III], but there are few data on the efficacy of specific agents. Benzodiazepines are not recommended for other than brief use because of risks of daytime sedation, tolerance, rebound insomnia, worsening cognition, falls, disinhibition, and delirium [II].

Diphenhydramine is not recommended because of its anticholinergic properties [II].

Antipsychotic medications should not be used solely for the purpose of treating sleep disturbances [I].

#### **NICE (2011)**

The review and re-appraisal of donepezil, galantamine, rivastigmine and memantine for the treatment of AD has resulted in a change in the guidance. Specifically:

- Donepezil, galantamine and rivastigmine are now recommended as options for managing mild as well as moderate AD, **and**
- Memantine is now recommended as an option for managing moderate AD for people who cannot take acetylcholinesterase (AChE) inhibitors, and as an option for managing severe AD.

#### **Guidance**

The three AChE inhibitors donepezil, galantamine, and rivastigmine are recommended as options for managing mild to moderate AD under all of the conditions specified below.

Memantine is recommended as an option for managing AD for people with:

- Moderate AD who are intolerant of or have a contraindication to AChE inhibitors or
- Severe AD

Treatment should be under the following conditions:

- Only specialists in the care of people with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of the older people) should initiate treatment. Carers' views on the patient's

condition at baseline should be sought.

- Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.
- Patients who continue on treatment should be reviewed regularly using cognitive, global, functional, and behavioural assessment. Treatment should be reviewed by an appropriate specialist team, unless there are locally agreed protocols for shared care. Carers' views on the patient's condition at follow-up should be sought.

If prescribing an AChE inhibitor (donepezil, galantamine or rivastigmine), treatment should normally be started with the drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started). However, an alternative AChE inhibitor could be prescribed if it is considered appropriate when taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles.

When using assessment scales to determine the severity of AD, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the results and make any adjustments they consider appropriate. Healthcare professionals should also be mindful of the need to secure equality of access to treatment for patients from different ethnic groups, in particular those from different cultural backgrounds.

When assessing the severity of AD and the need for treatment, healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so. These include:

- If the cognition score is not, or is not by itself, a clinically appropriate tool for assessing the severity of that patient's dementia because of the patient's learning difficulties or other disabilities (for example, sensory impairments), linguistic or other communication difficulties or level of education or
- If it is not possible to apply the tool in a language in which the patient is sufficiently fluent for it to be appropriate for assessing the severity of dementia or
- If there are other similar reasons why using a cognition score, or the score alone, would be inappropriate for assessing the severity of dementia.

In such cases healthcare professionals should determine the need for initiation or continuation of treatment by using another appropriate method of assessment.

**SMOH  
(2007)**

### **Pharmacological Management of Dementia**

**GPP** - Pharmacotherapy should be part of a multi-pronged strategy to dementia management that encompasses a well-established diagnosis, education of patient and caregiver, non-pharmacological measures and comprehensive caregiver psychosocial intervention. (**GPP**)

**B** - Although high dose vitamin E (2000 IU per day) may have a modest effect in delaying disease progression in moderately severe AD, doses of vitamin E in excess of 400 IU a day should be avoided for the treatment of AD until there is further data on its safety, especially in patients with cardiovascular disease. (**Grade B, Level 1+**)

**A** - Anti-inflammatory agents (such as non-steroidal anti-inflammatory agents and cyclooxygenase 2 inhibitors) are not recommended for the prevention of cognitive decline in AD (Aisen et al., 2003; Reines et al., 2004). (**Grade A, Level 1++**)

**B** - Prednisolone is not recommended for the prevention of cognitive decline in AD (Aisen et al., 2000). (**Grade B, Level 1+**)

**A** - Oestrogen is not recommended for the prevention of cognitive decline in women with dementia. (**Grade A, Level 1++**)

**A** - Acetylcholinesterase inhibitors should be considered for the management of all patients with mild to moderate AD. (**Grade A, Level 1++**)

**B** - Acetylcholinesterase inhibitors can be considered for the management of moderate to severe AD. (**Grade B, Level 1+**)

**A** - Acetylcholinesterase inhibitors have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia. (**Grade A, Level 1+**)

**B** - Acetylcholinesterase inhibitors can be considered for the management of dementia with Lewy bodies and Parkinson's disease dementia. (**Grade B, Level 1+**)

**B** - All three available acetylcholinesterase inhibitors (donepezil, rivastigmine and galantamine) can be considered for the pharmacological management of dementia, since there is no definite evidence to support a difference in clinical efficacy between them. (**Grade B, Level 1+**)

**A** - Where tolerated, acetylcholinesterase inhibitors should be titrated to recommended doses (5 to 10 mg/day donepezil; 6 to 12 mg/day rivastigmine; 16 to 24 mg/day galantamine), which have been shown to confer greater benefit compared with lower doses. (**Grade A, Level 1++**)

**B** - NMDA antagonists such as memantine can be considered for the management of moderate to severe AD, either alone or in combination with acetylcholinesterase inhibitors. **(Grade B, Level 1+)**

**B** - NMDA antagonists such as memantine may be a treatment option for mild to moderate AD, if acetylcholinesterase inhibitor therapy is contra-indicated, not tolerated or if there is disease progression despite an adequate trial of acetylcholinesterase inhibitor. **(Grade B, Level 1+)**

**A** - NMDA antagonists have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia. **(Grade A, Level 1+)**

**B** - Practitioners who prescribe ginkgo for the treatment of dementia should be aware of the unestablished benefit, variability of active ingredient among preparations, and potential for drug interactions. **(Grade B, Level 1+)**

**A** - Selegiline is not recommended for the treatment of core or associated symptoms in AD. (Birks & Flicker, 2003) **(Grade A, Level 1++)**

**GPP** - Appropriate treatment of vascular risk factors is recommended for all patients. However, it should be noted that whilst promising observational data exists, it remains to be shown in a randomised controlled clinical trial if any prevention strategy such as blood pressure reduction or antiplatelet treatment for the secondary prevention of stroke, will reduce the incidence of vascular dementia. **(GPP)**

**GPP** - The decision to initiate costly symptomatic dementia treatment, such as acetylcholinesterase inhibitors or NMDA antagonists, should always be made in consultation with the patient and family after careful consideration of the expected magnitude of benefit, side effects, comorbidities and costs of treatment. **(GPP)**

**GPP** - Patients who are started on acetylcholinesterase inhibitors or NMDA antagonists should be carefully monitored for side effects and response to treatment. **(GPP)**

#### **Pharmacological Interventions to Manage Behavioural and Psychological Symptoms of Dementia (BPSD)**

**GPP** - Antidepressants may be used for the treatment of comorbid depression in dementia provided their use has been evaluated carefully for each patient. **(GPP)**

**A** - Conventional and atypical antipsychotics may be used with caution, given their side effect profile, to treat neuropsychiatric symptoms of dementia. **(Grade A, Level 1+)**

**B** - Trazodone may be considered for patients with depressive symptoms and dementia

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|  | <p>associated agitation. (<b>Grade B, Level 1+</b>)</p> <p><b>A</b> - Routine use of mood stabilizers, such as carbamazepine and sodium valproate, is not recommended for treatment of behavioural symptoms associated with dementia. (<b>Grade A, Level 1+</b>)</p> <p><b>GPP</b> - An individualized approach to managing behavioural problems in dementia patients is required. (<b>LGPP</b>)</p> <p><b>GPP</b> - Cholinesterase inhibitor therapy may be considered in treatment of patients with behavioural problems if antipsychotics are inappropriate. (<b>GPP</b>)</p> <p><b>GPP</b> - The decision to start antipsychotic therapy to control behavioural problems in dementia patients should be made in consultation with the patient and family, after careful consideration of the benefit, adverse-effects and co-morbidities. (<b>GPP</b>)</p> <p><b>B</b> - For patients with dementia with Lewy Body and behavioural problems, acetylcholinesterase inhibitors should be considered first for management of the behavioural problems. (<b>Grade B, Level 1+</b>)</p> <p><b>GPP</b> - In all patients started on antipsychotic medication, they should be monitored carefully for side effects and response to treatment. In patients who are stable, antipsychotic withdrawal should be considered. (<b>GPP</b>)</p> |
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Patient and Caregiver Education (Back to top)

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|----------------------------|--|
| <b>ACP/AAFP<br/>(2008)</b> | No recommendations offered.  |
| <b>APA<br/>(2007)</b>      | <p><b>Psychiatric Management</b></p> <p>Important aspects of psychiatric management include educating patients and families about the illness, its treatment, and sources of additional care and support (e.g., support groups, respite care, nursing homes, and other long-term-care facilities) and advising patients and their families of the need for financial and legal planning due to the patient's eventual incapacity (e.g., power of attorney for medical and financial decisions, an up-to-date will, and the cost of long-term care) [<b>I</b>].</p> |
| <b>NICE<br/>(2011)</b>     | No recommendations offered.  |

| <b>SMOH<br/>(2007)</b>  | No recommendations offered.  |  |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
|---|--|--|--|---|--|--|----------------------------|-----------------------------------|--|--|---|--|------|--------|------|----------|--------|------|-----|--------|------|--|------------------|--|
| <b>ACP/AAFP<br/>(2008)</b>  | <table border="1"> <thead> <tr> <th colspan="3" data-bbox="365 325 901 430"> <b>American College of Physicians' Clinical Practice Guidelines Grading System*</b> </th> </tr> <tr> <th data-bbox="365 430 544 535"> <b>Quality of Evidence</b> </th> <th colspan="2" data-bbox="544 430 901 535"> <b>Strength of Recommendation</b> </th> </tr> </thead> <tbody> <tr> <td data-bbox="365 535 544 861"></td> <td data-bbox="544 535 747 861">           Benefits Clearly Outweigh Risks and Burden <b>OR</b> Risks and Burden Clearly Outweigh Benefits         </td> <td data-bbox="747 535 901 861">           Benefits Finely Balanced with Risks and Burden         </td> </tr> <tr> <td data-bbox="365 861 544 913">           High         </td> <td data-bbox="544 861 747 913">           Strong         </td> <td data-bbox="747 861 901 913">           Weak         </td> </tr> <tr> <td data-bbox="365 913 544 976">           Moderate         </td> <td data-bbox="544 913 747 976">           Strong         </td> <td data-bbox="747 913 901 976">           Weak         </td> </tr> <tr> <td data-bbox="365 976 544 1039">           Low         </td> <td data-bbox="544 976 747 1039">           Strong         </td> <td data-bbox="747 976 901 1039">           Weak         </td> </tr> <tr> <td data-bbox="365 1039 544 1281">           Insufficient evidence to determine net benefits or risks         </td> <td colspan="2" data-bbox="544 1039 901 1281">           I recommendation         </td> </tr> </tbody> </table> <p data-bbox="349 1302 1466 1386">           *Adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup.         </p> |  |  | <b>American College of Physicians' Clinical Practice Guidelines Grading System*</b> |  |  | <b>Quality of Evidence</b> | <b>Strength of Recommendation</b> |  |  | Benefits Clearly Outweigh Risks and Burden <b>OR</b> Risks and Burden Clearly Outweigh Benefits | Benefits Finely Balanced with Risks and Burden | High | Strong | Weak | Moderate | Strong | Weak | Low | Strong | Weak | Insufficient evidence to determine net benefits or risks | I recommendation |  |
| <b>American College of Physicians' Clinical Practice Guidelines Grading System*</b> |  |  |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
| <b>Quality of Evidence</b>  | <b>Strength of Recommendation</b>  |  |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
|   | Benefits Clearly Outweigh Risks and Burden <b>OR</b> Risks and Burden Clearly Outweigh Benefits  | Benefits Finely Balanced with Risks and Burden |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
| High  | Strong   | Weak   |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
| Moderate  | Strong   | Weak   |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
| Low   | Strong   | Weak   |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
| Insufficient evidence to determine net benefits or risks                            | I recommendation   |  |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |
| <b>APA<br/>(2007)</b>   | <p data-bbox="349 1459 1466 1501">           Definition of the Three Categories of Endorsement         </p> <p data-bbox="349 1522 1466 1564">           [I] Recommended with substantial clinical confidence         </p> <p data-bbox="349 1585 1466 1627">           [II] Recommended with moderate clinical confidence         </p> <p data-bbox="349 1648 1466 1690">           [III] May be recommended on the basis of individual circumstances         </p> <p data-bbox="349 1711 1466 1753">           Nature of Supporting Evidence         </p> <p data-bbox="349 1774 1466 1816">           [A] Double-blind, randomized clinical trial. A study of an intervention in which subjects are         </p>  |  |  |   |  |  |                            |                                   |  |  |   |  |      |        |      |          |        |      |     |        |      |  |                  |  |

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|                               | <p>prospectively followed over time; there are treatment and control groups; subjects are randomly assigned to the two groups; both the subjects and the investigators are blind to the assignments.</p> <p>[A-] Randomized clinical trial. Same as above, but not double-blind.</p> <p>[B] Clinical trial. A prospective study in which an intervention is made and the results of that intervention are tracked longitudinally; study does not meet standards for a randomized clinical trial.</p> <p>[C] Cohort or longitudinal study. A study in which subjects are prospectively followed over time without any specific intervention.</p> <p>[D] Case-control study. A study in which a group of patients is identified in the present and information about them is pursued retrospectively or backward in time.</p> <p>[E] Review with secondary data analysis. A structured analytic review of existing data, e.g., a meta-analysis or a decision analysis.</p> <p>[F] Review. A qualitative review and discussion of previously published literature without a quantitative synthesis of the data.</p> <p>[G] Other. Textbooks, expert opinion, case reports, and other reports not included above.</p> |
| <p><b>NICE<br/>(2011)</b></p> | <p>Not applicable</p>   |
| <p><b>SMOH<br/>(2007)</b></p> | <p>Levels of Evidence</p> <p>1++ High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias</p> <p>1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias</p> <p>1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias</p> <p>2++ High quality systematic reviews of case-control or cohort or studies<br/>High quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</p> <p>2+ Well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</p> <p>2- Case-control or cohort studies with a high risk of confounding or bias and a significant risk</p>   |

that the relationship is not causal

3 Non-analytic studies e.g., case reports, case series

4 Expert opinion

Grades of Recommendation

A. At least one meta-analysis, systematic review, or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target population; or

A body of evidence, consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B. A body of evidence, including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C. A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D. Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

GPP (good practice points) Recommended best practice based on the clinical experience of the guideline development group.

## Methodology

| <b>ACP/AAFP<br/>(2008)</b>  | <b>APA<br/>(2007)</b> | <b>NICE<br/>(2011)</b> | <b>SMOH<br/>(2007)</b> |
|---|-----------------------|------------------------|------------------------|
| <p>To collect the evidence, all four groups performed searches of electronic databases. ACP/AAFP and NICE also performed hand-searches of published literature; NICE also searched unpublished data. All of the groups, with the exception of SMOH, provide details of the literature selection/collection process, including the</p> |                       |                        |                        |

names of databases used, date ranges searched, and search terms employed. Two of the groups, ACP/AAFP and NICE, differ from the others in that they commissioned external, independent systematic reviews. ACP/AAFP recommendations are based on a systematic evidence review by Raina and colleagues and the Agency for Healthcare Research and Quality-sponsored McMaster University Evidence-based Practice Center. The NICE assessment report for its technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG).

To assess the quality and strength of the selected evidence, ACP/AAFP and SMOH weighted it according to a rating scheme and provide the scheme. NICE employed expert consensus; APA does not state the methods used. With regard to evidence analysis, all four groups reviewed published meta-analyses and performed a systematic review. All of the systematic reviews, with the exception of SMOH's, incorporated evidence tables. NICE and ACP/AAFP are the only two groups to perform their own meta-analysis. A description of the methods used to analyze the evidence is provided by ACP/AAFP and NICE.

All four groups employed expert consensus to develop the recommendations and provide a description of the process. Moreover, all of the groups, with the exception of NICE, rate the strength of the recommendations according to a scheme. Concerning issues of cost, ACP/AAFP and NICE reviewed published cost analyses; NICE undertook additional cost analyses of its own. See the original guideline document for details of the cost analysis. To validate the guidelines, ACP/AAFP, APA, and NICE sought either internal peer review, external peer review, or both. SMOH does not provide information regarding any methods used to validate its guideline.

## Sources of Funding

|                            |   |
|----------------------------|---|
| <b>ACP/AAFP<br/>(2008)</b> | American College of Physicians<br>American Academy of Family Physicians |
| <b>APA<br/>(2007)</b>      | American Psychiatric Association  |
| <b>NICE<br/>(2011)</b>     | National Institute for Health and Clinical Excellence                   |
| <b>SMOH<br/>(2007)</b>     | Singapore Ministry of Health  |

## Benefits

|                            |  |
|----------------------------|--|
| <b>ACP/AAFP<br/>(2008)</b> | <p>Appropriate pharmacologic treatment of dementia based on tolerability, adverse effect profile, ease of use, and cost of medications</p> |
| <b>APA<br/>(2007)</b>      | <p>Effective treatment and management of patients with AD and other dementias</p>  |
| <b>NICE<br/>(2011)</b>     | <p>Appropriate use of donepezil, galantamine, rivastigmine and memantine for the treatment of patients with AD</p>                         |
| <b>SMOH<br/>(2007)</b>     | <p>Appropriate assessment, evaluation, and management of patients with dementia</p>  |

## Harms

|                            |   |
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| <b>ACP/AAFP<br/>(2008)</b> | <p><b>Adverse Effects of Medications</b></p> <ul style="list-style-type: none"> <li> <b>Donepezil:</b> Withdrawal rates because of adverse events associated with donepezil ranged from 0% to 57% in the treatment groups (0% to 20% in placebo groups). No study showed a statistically significant difference between the treatment and placebo groups for serious adverse events except for the expected side effects of cholinesterase inhibitors (diarrhea, nausea, and vomiting). Six studies reported a dose-response effect with increasing frequency of adverse events as dosage increased.         </li> <li> <b>Galantamine:</b> Withdrawal for adverse events for galantamine ranged from 8% to 54% in the treatment group (4% to 17% in the placebo group). Four studies showed a dose-response relationship for adverse events during titration. Although most trials did not report statistical analysis of adverse effects, 2 studies reported statistically significant weight loss in the treatment group. Commonly reported adverse effects included gastrointestinal symptoms (nausea, vomiting, and diarrhea), eating disorders/weight         </li> </ul> |
|----------------------------|---|

loss, and dizziness.

- **Rivastigmine:** Withdrawal rates related to adverse events ranged from 12% to 29% in the treatment group (0% to 11% in the placebo group). The frequency of adverse events between treatment and control groups did not differ. However, 2 studies showed a dose-response relationship for adverse events. The types of adverse events were consistent with those related to cholinesterase inhibitor use and included dizziness, nausea, vomiting, eating disorder/weight loss, and headache.
- **Tacrine:** The withdrawal rate related to adverse events ranged from 0% to 55% in the treatment group (0% to 12% in the placebo group). The evidence showed that adverse events related to tacrine were serious and increased with higher doses. Elevated alanine aminotransferase level and other hepatic abnormalities were reported in 6 of 7 studies. Nausea, vomiting, gastrointestinal problems, and dizziness were reported in addition to the serious liver abnormalities.
- **Memantine:** The withdrawal rates related to adverse effects varied from 9% to 12% in the treatment group (7% to 13% in the placebo group), including nausea, dizziness, diarrhea, and agitation.

Refer to the original guideline document for more information on adverse effects of medications.

**APA  
(2007)**

### **Psychosocial Treatment**

Short-term adverse emotional consequences have occasionally been reported with some psychosocial treatments. This is especially true of the cognitively oriented treatments, during which frustration, catastrophic reactions, agitation, and depression have been reported.

### **Pharmacological Treatment**

Certain medication side effects pose particular problems for elderly patients and those with dementia; medications with these side effects must therefore be used judiciously.

Anticholinergic side effects may be more burdensome for elderly patients owing to coexisting cardiovascular disease, prostate or bladder disease, or other general medical conditions.

These medications may also lead to worsening cognitive impairment, confusion, or even delirium. Orthostasis is common in elderly patients because of decreased vascular tone and medication side effects. As a result, elderly patients, especially those with dementia, are more prone to falls and associated injuries. Medications associated with central nervous system sedation may worsen cognition, increase the risk of falls, and put patients with sleep apnea at risk for additional respiratory depression. Finally, elderly patients, especially those

with AD, Parkinson's disease, or dementia with Lewy bodies, are especially susceptible to extrapyramidal side effects.

Side effects of specific medications are discussed further in the original guideline document.

**NICE  
(2011)**

- Common undesirable effects of donepezil include diarrhoea, muscle cramps, fatigue, nausea, vomiting and insomnia.
- Common undesirable effects of galantamine and rivastigmine are mainly gastrointestinal including nausea and vomiting.
- Common undesirable effects of memantine are dizziness, headache, constipation, somnolence and hypertension.

For full details of side effects and contraindications, see the Summaries of Product Characteristics.

**SMOH  
(2007)**

#### **Adverse Effects of Medications**

- Although generally well tolerated, dose-related gastrointestinal side effects (nausea, vomiting, diarrhea, anorexia) are common with *acetylcholinesterase inhibitor (AChEI)* use. These are transient and often circumvented to a large extent by a slower titration and taking the medication with food. Great caution should be exercised in those with bradycardia, sick sinus syndrome or cardiac conduction disturbances, in view of possible adverse effects of symptomatic bradycardia and syncope. Other less common side effects that have been reported include muscle cramps, insomnia, vivid dreams and weight loss. Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD) patients commenced on AChEI should be carefully monitored for worsening of motor symptoms.
- Compared with AChEI, gastrointestinal-related side effects are uncommon with *memantine* use. Common adverse events of memantine include dizziness, headache, fatigue, hallucinations and confusion, but these tend to be transient. Memantine should be used with caution in patients with epilepsy and renal impairment, and the clinician should be aware of interactions involving commonly prescribed medications such as dextromethorphan and L-dopa.
- Doses of *vitamin E* in excess of 400 IU a day should be avoided for the treatment of AD until there is further data on its safety, especially in patients with cardiovascular disease.
- *Conventional antipsychotics* are associated with extrapyramidal side effects and

|  |   |
|--|---|
|  | <p>somnolence.</p> <ul style="list-style-type: none"> <li>• <i>Atypical antipsychotics</i> are associated with somnolence and gait disturbance. These adverse effects are 7.5 to 11 times more common in olanzapine-treated group compared to placebo. Serious adverse events occurred in 16.8% of risperidone versus 8.8% of placebo group, including 5 strokes and 1 transient ischaemic attack, all in risperidone group. Meta-analysis of adverse events performed showed 3-fold statistically increased risk of cerebrovascular adverse events with risperidone and olanzapine (no statistically significant increase in mortality) while another meta-analysis comparing risk of death with atypical antipsychotics (aripiprazole, olanzapine, risperidone and quetiapine) with placebo showed increased risk of death. Other serious adverse events reported included somnolence and metabolic complications of hyperglycemia and weight gain.</li> <li>• A recent retrospective cohort study had shown increased mortality among subjects using <i>conventional antipsychotics</i> compared to atypical antipsychotics. Antipsychotic medication should be used cautiously in patients suspected to have dementia with Lewy Body as these patients have marked sensitivity to neuroleptic agents, including life-threatening neuroleptic malignant syndrome.</li> </ul> |
|--|---|

## Contraindications

|                            |  |
|----------------------------|--|
| <b>ACP/AAFP<br/>(2008)</b> | Major contraindications of cholinesterase inhibitors and memantine include, but are not limited to, uncontrolled asthma, angle-closure glaucoma, the sick sinus syndrome, and left bundle-branch block.  |
| <b>APA<br/>(2007)</b>      | <ul style="list-style-type: none"> <li>• Side effects occur infrequently with cholinesterase inhibitors, but bradycardia should be considered a relative contraindication to their use.</li> <li>• The main contraindication to use of cholinesterase inhibitors is hypersensitivity to the individual drugs.</li> <li>• Sleep apnea is a relative contraindication to the use of benzodiazepines or other agents that suppress respiratory drive.</li> <li>• Selegiline use is considered contraindicated in combination with meperidine, SSRIs, or tricyclic antidepressants.</li> </ul> |
| <b>NICE<br/>(2011)</b>     | For full details of side effects and contraindications, see the Summaries of Product   |

|                        |                  |
|------------------------|------------------|
|                        | Characteristics. |
| <b>SMOH<br/>(2007)</b> | Not stated       |

## Abbreviations

ACP/AAFP, American College of Physicians/American Academy of Family Physicians

AD, Alzheimer's disease

APA, American Psychiatric Association

FDA, U.S. Food and Drug Administration

NICE, National Institute for Health and Clinical Excellence

NMDA, N-methyl-D-aspartate

NSAID, nonsteroidal anti-inflammatory agents

SMOH, Singapore Ministry of Health

SSRI, selective serotonin reuptake inhibitor

## Status

This synthesis was prepared by ECRI on September 27, 2006. It was reviewed by SIGN on October 23, 2006 and CWGAD/AALA on October 26, 2006. This synthesis was revised on November 26, 2007 following the removal of the CWGAD/AALA recommendations from the Web site. This synthesis was updated on May 12, 2008 to include ACP/AAFP, APA and SMOH recommendations. The updated recommendations were verified by ACP on May 27, 2008 and by APA on June 23, 2008. This synthesis was updated in June 2010 to add NICE recommendations. This synthesis was updated in March 2012 to remove SIGN recommendations and update NICE recommendations.





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June 18, 2012

Dear Medical Director,

Over the past few months, AMDA-Dedicated to Long Term Care Medicine has partnered with the Centers for Medicare & Medicaid Services (CMS), as well as several other organizations, in an effort to improve care provided to nursing home residents with dementia under a new, joint behavioral health initiative.

Dementia can significantly impair a resident's ability to effectively communicate his/her needs and concerns. Communication attempts may appear as behaviors that are disruptive or distressing. It is therefore essential to gain an understanding of what is driving these behaviors prior to initiating an intervention or treatment. Sometimes these behaviors may result from an undiagnosed medical condition, an adverse reaction to medication, unmet physical need, or mental illness.

In April 2011 the Department of Health and Human Services Office of Inspector General (OIG) released the report, *Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents* (<http://oig.hhs.gov/oei/reports/oei-07-08-00150.pdf>). The report found that in some circumstances antipsychotic medications are being prescribed in an attempt to manage the behaviors of patients with dementia and psychological symptoms, but who did not have an approved indication for their use. While off label prescribing in this context does not always constitute inappropriate prescribing, use of antipsychotic drugs do have significant health risks in this population. This report, and other recent reports, has led to heightened regulatory, legislative, and consumer awareness of the potential dangers these medications may cause for individuals with dementia. Such efforts also complement the recently released, *Draft Framework for the National Plan to Address Alzheimer's Disease* by the U.S. Department of Health and Human Services.

**We are asking you, as the medical director of your facility, to join with AMDA and CMS, in the nationwide effort to reduce the unnecessary use of antipsychotic agents by refocusing the interdisciplinary team on a better understanding of the root cause of dementia related behaviors.**

**In this regard, we encourage you to share and discuss the following information with your facility.**

### Medical Director's Role as Clinical Leader in Dementia Care

The medical director leads the team that provides the clinical care to the residents in the facility. In that role, medical directors should help to implement policies and procedures that promote a process of person-centered care, learning "the story" behind each resident, evaluating the behavior changes and excluding potential medical causes of behavioral symptoms. If policies are already in place, the medical director should help to educate the team in existing policies and procedures and ensure that those policies have been implemented. Nursing home policies should direct the staff to identify resident-specific needs, optimize choices, and promote consistent assignment so that staff knows residents well enough to meet their specific care needs. Education should foster the staff's understanding of dementia-related behavior as a form of communication.

Policies should also promote staff's ability to identify relevant risks to any medication, provide parameters for monitoring medications, and institute a process for staff and prescriber reassessment of the resident's response to treatment over time. While there is an established, evidence-based role for antipsychotic medications in managing psychoses, such as schizophrenia and bipolar mania, we are concerned about potential unnecessary use of these medications in persons with behavioral and psychological symptoms related to dementia (BPSD). Medical directors are encouraged to educate facility staff, residents and families about appropriate use of antipsychotic medications, and to begin an ongoing dialogue and collaboration that focuses on non-pharmacologic interventions and person-centered dementia care for BPSD. Educational efforts should also address proper monitoring and the tapering of antipsychotic drugs when used.

As part of the facility's Quality Assessment and Assurance Committee, the medical director along with the administrator, consultant pharmacist and director of nursing should assist the facility with a review of the processes of care for those residents with BPSD on antipsychotic medications. Questions medical directors often ask during the review include the following:

- How many residents in the facility with BPSD receive antipsychotic medications and how is the use monitored?
- What is the process in the facility to initiate the use of these medications?
- What is the process for gradual dose reduction and discontinuation of these medications?
- How is the resident/family/or legal representative informed of the risks and benefits of the use of these medications? How are these discussions documented?

### Use of An Interdisciplinary Team

One effective practice for monitoring the use of antipsychotic medications in a facility used by several of our AMDA members is to have the medical director work closely with an interdisciplinary team composed of nursing, social services, therapeutic recreation specialist and a pharmacist. This team meets regularly to review psychotropic drug use. Individual residents are discussed by the team during their quarterly assessments, or with initiation of psychotropic medications, or when there has been a change in the condition of a resident taking a psychotropic medication. During the meeting, the care plans and medical records are reviewed and resident's functional status, medications, presence of medication side effects and presence or absence of achieved goals for medication use are discussed. This practice emphasizes person-centered care. Recommendations from the interdisciplinary team are then made to or with the resident's attending physician. The team tracks the recommendations for acceptance by the primary care providers and effectiveness in the quality of care for the

resident. This information is further reviewed by the facility Quality Assessment and Assurance Committee for effectiveness in addressing the needs of the residents in the facility.

AMDA has developed comprehensive resources to assist medical directors with these issues. These include talking points, a medication management manual, clinical practice guidelines, a series of webinars, and a handbook for nursing home staff. A complete listing of AMDA resources is attached to this letter.

AMDA looks forward to working with you to improve long term care by standardizing our practices, educating the interdisciplinary care team, further developing strong relationships with residents and their advocates, and supporting caregivers in long term care. Increased prescriber training will help reduce unnecessary antipsychotic drug prescribing. AMDA looks forward to an ongoing collaboration with its medical directors.

Sincerely,



Matthew S. Wayne, MD, CMD  
President AMDA

#### AMDA Resources

- In 2011, AMDA released a series of talking points entitled "Appropriate Prescribing of Antipsychotics" to help minimize the *potential for inappropriate prescribing of psychoactive medications* ([http://www.amda.com/advocacy/AMDA\\_Antipsychotics\\_Tlkg\\_Pts.pdf](http://www.amda.com/advocacy/AMDA_Antipsychotics_Tlkg_Pts.pdf)).
- AMDA has several tools for clinical use in the nursing home including:
  - Clinical Practice Guidelines: To establish best practices for medical staff, AMDA has developed clinical practice guidelines on dementia, delirium, and acute problematic behavior for use as evidence-based tools to guide care.
    - <http://www.amda.com/tools/guidelines.cfm>
  - *Mental Health Documentation in the Nursing Home and Practical Psychiatry in the Long Term Care Home: A Handbook for Staff*, which is aimed at educating nursing and other staff.
    - <http://www.amda.com/tools/mentalhealth.cfm>
  - *Multidisciplinary Medication Management Manual*, provides practitioners in long term care with information and tools to help them improve patient care, enhance medication management, and reduce medication errors. This manual includes a chapter on appropriate prescribing of psychoactive agents in the long term care setting, which is designed to help guide physicians regarding such issues as the clinical and regulatory documentation necessary when residents are prescribed psychoactive medications.
    - <http://www.amda.com/resources/print.cfm#MED>

- AMDA has hosted a series of educational Webinars on the issue including:
  - *Medication Management: the Doc, F329, and the OIG*. The learning objectives for this webinar included: delineating medication management as it is regulated in nursing homes; discussing the May 2011 report by the OIG concerning psychotropic drug use in nursing homes; and discussing roles of the medical director and physicians practicing in long term care concerning optimizing medication management for nursing home resident.
    - <http://www.amda.com/cmefirect/webinars/web1106E.cfm>
  - AMDA's eUniversity is hosting a webinar on June 28th, titled *Medication Management: Antipsychotic Drug Use Reduction 2012*. To learn more and register, visit, <http://www.amda.com/cmefirect/webinars/web1206E.cfm>.
  - *Use of Psychoactive Medications with Special Emphasis on Antipsychotics in the Long-Term Care Setting*. The learning objectives for this webinar included: recognizing how to analyze and evaluate problematic behavior vs. behavioral symptoms related to dementia; discussing approaches to changing or removing triggers for problematic behavior with non-pharmacological approaches; and describing the appropriate use of psychoactive agents in the long-term care setting.
    - <http://www.prolibraries.com/amda/?select=session&sessionID=773>
  - *The True Meaning of Non-Pharmacologic Management of Behavioral Symptoms in Older Adults with Cognitive Impairment* emphasized the use of non-pharmacologic interventions as the first-line approach to managing disruptive and/or potentially dangerous behavioral symptoms in persons with dementia. The webinar provided a comprehensive, multi-disciplinary approach to these challenging clinical situations and also provided participants with knowledge enabling them to effectively design and implement non-pharmacologic interventions in their facilities.
    - [http://amda.networkats.com/members\\_online/members/viewitem.asp?item=WEB1112E&catalog=SELF&pn=1&af=AMDA](http://amda.networkats.com/members_online/members/viewitem.asp?item=WEB1112E&catalog=SELF&pn=1&af=AMDA)
- More resources on this topic are also located here: <http://www.amda.com/advocacy/brucbs.cfm>