1. **Aim/Purpose of this Guideline**
   1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of donepezil, galantamine, rivastigmine, and memantine.

2. **The Guidance**
   2.1. See below for the Shared Care Guideline.
This shared care guideline sets out details for the sharing of care of adults with dementia prescribed donepezil, galantamine, rivastigmine, and memantine. These guidelines provide additional limited information necessary to aid in the treatment of these patients. As with all shared care guidelines they highlight relevant prescribing issues but should be used in conjunction with relevant NICE guidance, the BNF, ABPI summary of product characteristics and do not replace them.

INTRODUCTION / BACKGROUND INFORMATION

Dementia is a chronic progressive organic mental disorder in which there is disturbance of multiple higher cortical functions. Alzheimer’s disease (AD) is the commonest cause of dementia and is characterised by an insidious onset and slow deterioration, which makes diagnosis difficult.

The UK incidence of Alzheimer’s disease in people over the age of 65 years is estimated to be 4.9 per 1000 person-years. Between 50 and 64% of people with Alzheimer’s disease are estimated to have mild to moderately severe disease, and approximately 50% have moderately severe to severe disease.

The severity of Alzheimer’s disease can be assessed using several methods, depending on the setting (for example research or clinical practice) and the outcome being assessed. Clinical practice uses a variety of measures, often along with clinically based assessments such as biographical interview. A range of generic cognitive screening tools is used to define severity of Alzheimer’s disease eg the mini-Addenbrooke Cognitive Examination (mini-ACE) is one such tool.

Acetylcholine (ACh) is a neurotransmitter that appears depleted in the brains of patients with AD. Acetylcholinesterase inhibitors elevate the levels of ACh by inhibiting an enzyme responsible for its breakdown leading to an improvement in symptoms for some patients though not altering the outcome of the disease. Memantine has a different mode of action by blocking the effects of pathologically elevated toxic levels of glutamate that may lead to neuronal dysfunction.

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE – AS PER NICE TAG 217 (MARCH 2011) AND CLINICAL GUIDELINE (NOVEMBER 2006)

- Healthcare professionals should not rely solely on the cognitive assessment score to assess the severity of Alzheimer’s disease when the patient has learning or other disabilities, or other communication difficulties. NICE guidelines suggest alternative rating scales for people with learning disabilities.
- In addition, donepezil, galantamine, and rivastigmine should be considered for people with mild, moderate or severe Alzheimer’s disease who have non-cognitive symptoms and/or behaviour that challenges causing significant distress or potential harm to the individual if non-pharmacological approach is inappropriate or has been ineffective, and antipsychotic drugs are inappropriate or have been ineffective.
- Acetylcholinesterase inhibitors should not be used for non-cognitive symptoms or behaviour that challenges in vascular dementia except as part of properly constructed clinical studies. Mixed cases of dementia (eg, Alzheimer’s disease and vascular dementia) may be considered for treatment.

Donepezil, galantamine and rivastigmine are recommended as options for mild to moderate Alzheimer’s disease under all of the conditions in the box below.

Memantine is recommended as an option for managing Alzheimer’s disease for people with:

- moderate Alzheimer’s disease who are intolerant of or have a contraindication to AChE inhibitors or
- severe Alzheimer’s disease.

Again, treatment should be under all of the conditions in the box below.

- Only specialists in the care of patients with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of older people) should decide that treatment should commence. This initial assessment may be undertaken by specialist memory assessment staff. Carers’ views on the patient’s condition at baseline should be sought.
- Patients who continue on the drug should be reviewed regularly (at least every 6 months) 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. Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional and behavioural symptoms.
PREPARATIONS AND DOSAGE
Donepezil standard tablet is the default first choice option, accepting there may be reasons why other drugs or other formulations may be chosen. The reason for recommending a drug other than donepezil should be included in the letter to the GP.

Donepezil - 5mg, 10mg standard tablet.
Initially 5mg once a day, increased if necessary after one month to 10mg once a day (maximum dose). The once daily dose may be of advantage to some patients/carers, e.g. if carers visit to administer medicines.

Galantamine – 8mg, 12mg tablet and M/R Capsule formulation 8mg, 16mg, 24mg.
Oral solution, sugar free, 4mg/ml.
Initially 4mg twice a day for four weeks, increasing to 8mg twice a day. Dose may be further increased to 12mg twice a day after four weeks.
M/R formulations initially 8mg once daily for four weeks increased to 16mg once daily for four weeks; maintenance 16-24mg daily.

Rivastigmine – 1.5mg, 3mg, 4.5mg, 6mg capsule and patch formulation 4.6mg/24 hours, 9.5mg/24 hours.
Initially 1.5mg twice a day, increased in steps of 1.5mg twice a day at intervals of at least two weeks, according to response and tolerance. Usual dose range is 3-6mg twice a day. Maximum dose is 6mg twice a day.
Patch formulation (ONLY if the patient has a swallowing problem): initially apply 4.6mg/24hours. Ensure patches are removed after 24 hours (MHRA warning) and resite a replacement patch on a different area (avoid using the same area for 14 days). If well tolerated increase to 9.5mg/24hours daily after no less than four weeks. If patch is not applied for more than several days, treatment should be restarted with 4.6mg/24hours patch.
Rivastigmine capsules are also licensed for mild to moderate dementia in Parkinson’s Disease and is included in the NICE guideline for Parkinson’s disease. The patch formulation is not so licensed.

Memantine - initiation packs, and 10mg, 20mg tablet, 10mg/ml oral solution.
Initially 5 mg once daily and increasing in steps of 5 mg at weekly intervals to a maximum of 20 mg daily.
Oral solution delivered by pump, 5mg/actuation dosed onto a spoon or into a glass of water.

CONTRAINDICATIONS
Galantamine is contraindicated in severe renal impairment and metabolic disorders of galactose metabolism. Donepezil, galantamine and rivastigmine are contraindicated in breastfeeding. Donepezil and rivastigmine are contraindicated in pregnancy. Memantine is contraindicated where there is a history of convulsions.

PRECAUTIONS
- Donepezil, galantamine and rivastigmine should be prescribed with care in patients with asthma and obtrusive airways disease, severe hepatic or renal failure, cardiovascular conditions, eg heart block or SVT, urinary outflow obstruction, or history of peptic ulceration. The specialist team may need to seek further advice in cases where the risk is unclear.
- Memantine should be used with caution in pregnancy, history of convulsions, renal impairment (avoid if eGFR is less than 5ml /minute/1.73m²)

MONITORING
SPECIALIST TEAM:
- The specialist team should review the patient at around 12 weeks to assess benefit and review the dose.
- After the initial treatment period, regular assessments with a maximum of 6 months gap should be carried out by the specialist team using consistent methods and should include assessment of cognitive, global and behavioural functioning and activities of daily living. This should allow for comparison over time. These assessments may be undertaken by trained health care assistants or primary care dementia liaison nurses.
- Following each assessment, the drug should normally only be continued if above the relevant threshold for that assessment tool, and the patient’s global, functional and behavioural condition remains at a level where the drug is considered to be having a worthwhile effect. If the patient does not clearly benefit from the drug treatment, when assessed by the agreed measures, the specialist should recommend discontinuation of the drug at a review consultation.

GENERAL PRACTICE:
- There are no specific biochemical monitoring requirements for the GP to undertake.

SIDE EFFECTS
Below are some of the more common side effects. Please note that this list is NOT exhaustive and that it is recommended that the SPC and BNF should be consulted for a more comprehensive list.

Donepezil, galantamine and rivastigmine can cause unwanted dose-related cholinergic effects and should be started at a low dose. The dose should be increased incrementally according to response and tolerability. Adverse effects could include:
- Nausea and vomiting.
Abdominal disturbances (including diarrhoea and abdominal pain).
- Weight loss.
- Dizziness.
- Tremor.
- Sweating.
- Asthenia.
- Fatigue
- Insomnia

They are usually worse at higher doses and during rapid dose titration.

Memantine common adverse effects are:
- Dizziness,
- Headache
- Constipation
- Somnolence
- Hypertension

COMMON/SIGNIFICANT DRUG INTERACTIONS
The SPC and BNF should be consulted for a more comprehensive list of potential drug interactions.

Acetylcholinesterase inhibitors:
Concurrent therapy with the following should be treated with caution:

Enzyme Inhibitors:
• Itraconazole and ketoconazole, erythromycin, fluoxetine (with donepezil or galantamine).

Enzyme Inducers:
• Rifampicin, phenytoin, carbamazepine.

Other:
• Neuromuscular blockers, Beta-blockers, digoxin (with galantamine).

Donepezil, galantamine and rivastigmine have the potential to interfere with medications having anticholinergic activity.

Memantine:
The mode of action suggests that the effects of L-dopa, dopaminergic agonists, selegiline, and anticholinergics may be enhanced by concomitant treatment with NMDA-antagonists such as memantine.

The effects of barbiturates and neuroleptics may be reduced. Concomitant administration of memantine with the antispasmodic agents, dantrolene or baclofen, can modify their effects and a dosage adjustment may be necessary.

Concomitant use of memantine and amantadine should be avoided, owing to the risk of pharmacotoxic psychosis.

Possibly enhances anticoagulant effect of warfarin.

REFERENCES:
Summaries of Product Characteristics.
NICE Clinical Guideline 42 November 2006. Dementia
NICE Clinical Guideline 35 June 2006 Parkinson's Disease

Request for other formats
Please ask if you would like to receive this leaflet in large print, braille, on CD or in any other languages. If you would like the leaflet in an alternative format please contact the NHS Kernow Communications Team at communications@kernowcg.nhs.uk or call 01726 627800
AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of adult patients with dementia who are prescribed donepezil, galantamine, rivastigmine or memantine can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

In its guidelines on responsibility for prescribing (circular EL(91)127) between hospitals and GPs, the DH has advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

Specialist:

- Assess the patient, establish the diagnosis, determine a management strategy and devise a care plan in conjunction with the GP, other healthcare professionals and appropriate support agencies.
- Seek carer’s views on the condition of the person with dementia at baseline and make the carer aware of the nature of the effect of treatment and that it could be stopped.
- Recommend therapy with an acetylcholinesterase inhibitor - the decision as to which is the most appropriate product to use is the responsibility of the specialist, and should concur with current NICE Guidance, though donepezil is considered to be the default first choice.
- Send a letter to the GP, detailing the diagnosis, results of baseline assessments, name and dose of the prescribed drug treatment, clear schedule for any further dose titrations, contact details and arrangements for any further reviews.
- Where memantine is considered the treatment of choice, this should be initiated and prescribed by the specialist service. Following review of the patient at 4-6 weeks to assess whether the patient is tolerating memantine and complying with therapy, the GP may be asked if they are willing to participate in shared care.
- Liaise with CPN or care agencies as appropriate.
- All patients who have been initiated on cognitive enhancers will be followed up for review and on-going management by the specialist service on a needs led basis.
- Regularly review response to treatment using cognitive, global, functional and behavioural assessments and communicate the results of these to the patient’s GP.
- Prompt communication with GP of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.
- At the point when the treatment is considered not to be providing any further benefit in terms of its effect on cognitive, global, functional or behavioural functions, provide the GP with alternative suggestions on the future management of the patient.
- Reporting adverse events to the MHRA.

General Practitioner:

- Refer patients with suspected dementia to the specialist service after completing basic dementia screening as recommended in the NICE clinical guideline on dementia. Screening should include routine haematology, electrolytes, renal and liver function, thyroid function tests, serum B12, folate levels, mid stream urine and chest X-ray and ECG if deemed necessary.
- Notify the consultant in writing, without undue delay, if they do not agree to share care.
- Initiation of Donepezil / Galantamine / Rivastigmine after communication with specialists regarding the need for treatment, and continued prescribing of Memantine once the maintenance dose has been established by the specialist team.
- Ensure that shared care arrangements around monitoring and follow-up by specialists are in place.
- Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Arrange to review the patient on a regular basis to monitor their wellbeing.
- Avoid prescribing drugs with anticholinergic side effects, as these may reduce the efficacy of donepezil, galantamine and rivastigmine.
- Consider discontinuing treatment if no longer clinically effective, development of troublesome side effects or physical health issues that would preclude prescribing. GP to notify the specialist team if discontinuation occurs.
- Stopping treatment in the case of severe adverse event or as per shared care guideline.
- Reporting adverse events to the specialist and MHRA.

Patient: and parent / carer responsibilities

- Report any adverse effects to their GP and/or specialist regarding their treatment.
- Ensure that they have a clear understanding of their treatment and ensure they attend for monitoring requirements as per shared care guideline.
- Be aware that treatment may be stopped if patient does not attend for monitoring.

BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RELEVANT CLINICAL TEAM.
3. Monitoring compliance and effectiveness

<table>
<thead>
<tr>
<th>Element to be monitored</th>
<th>Compliance with prescribing and administration in accordance with this guideline (or other safe practice)</th>
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<tr>
<td>Lead</td>
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<tr>
<td>Tool</td>
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<tr>
<td>Frequency</td>
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<td>Reporting arrangements</td>
<td>Via Medicines Practice Committee</td>
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<tr>
<td>Acting on recommendations and Lead(s)</td>
<td>Relevant Clinical Staff</td>
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<tr>
<td>Change in practice and lessons to be shared</td>
<td>Relevant Clinical Staff</td>
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4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Diversity & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.
Appendix 1. Governance Information

<table>
<thead>
<tr>
<th>Document Title</th>
<th>Shared Care Guideline for the treatment of dementia</th>
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<tr>
<td>Date Issued/Approved:</td>
<td>January 2015</td>
</tr>
<tr>
<td>Date Valid From:</td>
<td>January 2015</td>
</tr>
<tr>
<td>Date Valid To:</td>
<td>February 2018</td>
</tr>
<tr>
<td>Directorate / Department responsible (author/owner):</td>
<td>Old Age Psychiatry / Eldercare / Learning Disabilities M Wilcock, Head of Prescribing Support Unit, Pharmacy Department, RCHT</td>
</tr>
<tr>
<td>Contact details:</td>
<td>01872 253548</td>
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<tr>
<td>Brief summary of contents</td>
<td>Some clinical issues and details of prescribing responsibilities for GP and specialists</td>
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<td>Suggested Keywords:</td>
<td>Shared care</td>
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<td></td>
<td>RCHT</td>
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<tr>
<td>Executive Director responsible for Policy:</td>
<td>Medical Director</td>
</tr>
<tr>
<td>Date revised:</td>
<td>January 2015</td>
</tr>
<tr>
<td>This document replaces (exact title of previous version):</td>
<td>Treatment of dementia – donepezil, galantamine, rivastigmine, and memantine</td>
</tr>
<tr>
<td>Approval route (names of committees)/consultation:</td>
<td>Cornwall Area Prescribing Committee</td>
</tr>
<tr>
<td>Divisional Manager confirming approval processes</td>
<td>Not required</td>
</tr>
<tr>
<td>Name and Post Title of additional signatories</td>
<td>Janet Gardner, Governance Lead CSSC</td>
</tr>
<tr>
<td>Signature of Executive Director giving approval</td>
<td>{Original Copy Signed}</td>
</tr>
<tr>
<td>Publication Location (refer to Policy on Policies – Approvals and Ratification):</td>
<td>Internet &amp; Intranet ✓ Intranet Only</td>
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<tr>
<td>Document Library Folder/Sub Folder</td>
<td>Clinical / Pharmacy</td>
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<td>Links to key external standards</td>
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<td>Related Documents:</td>
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<td>Training Need Identified?</td>
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Version Control Table

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<th>Date</th>
<th>Version No</th>
<th>Summary of Changes</th>
<th>Changes Made by (Name and Job Title)</th>
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<td></td>
<td>V2.0</td>
<td>Updated to comply with latest RCHT format</td>
<td>M Wilcock</td>
</tr>
<tr>
<td>Jan’15</td>
<td>V3.0</td>
<td>Changes to prescribing responsibilities and assessment tools</td>
<td>M Wilcock</td>
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All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.

This document is only valid on the day of printing

Controlled Document
This document has been created following the Royal Cornwall Hospitals NHS Trust Policy on Document Production. It should not be altered in any way without the express permission of the author or their Line Manager.
Appendix 2. Initial Equality Impact Assessment Screening Form

<table>
<thead>
<tr>
<th>Name of service, strategy, policy or project (hereafter referred to as policy) to be assessed: Shared care guideline for the treatment of dementia</th>
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</thead>
<tbody>
<tr>
<td>Directorate and service area: Pharmacy Is this a new or existing Procedure? Existing</td>
</tr>
<tr>
<td>Name of individual completing assessment: Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow Telephone: 01726 627953</td>
</tr>
<tr>
<td>1. Policy Aim*</td>
</tr>
<tr>
<td>2. Policy Objectives*</td>
</tr>
<tr>
<td>3. Policy – intended Outcomes*</td>
</tr>
<tr>
<td>5. How will you measure the outcome?</td>
</tr>
<tr>
<td>5. Who is intended to benefit from the Policy?</td>
</tr>
<tr>
<td>6a. Is consultation required with the workforce, equality groups, local interest groups etc. around this policy?</td>
</tr>
<tr>
<td>b. If yes, have these groups been consulted?</td>
</tr>
<tr>
<td>c. Please list any groups who have been consulted about this procedure.</td>
</tr>
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</table>

7. The Impact

Please complete the following table.

<table>
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<tr>
<th>Equality Strands:</th>
<th>Yes</th>
<th>No</th>
<th>Rationale for Assessment / Existing Evidence</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
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<tr>
<td>Sex (male, female, trans-gender / gender reassignment)</td>
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<tr>
<td>Race / Ethnic communities /groups</td>
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<tr>
<td>Disability - learning disability, physical disability, sensory impairment and mental health problems</td>
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<td>Religion / other beliefs</td>
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<td>Marriage and civil partnership</td>
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<td>Pregnancy and maternity</td>
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<td>Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian</td>
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You will need to continue to a full Equality Impact Assessment if the following have been highlighted:
- You have ticked “Yes” in any column above and
- No consultation or evidence of there being consultation - this excludes any policies which have been identified as not requiring consultation. or
- Major service redesign or development

8. Please indicate if a full equality analysis is recommended. | Yes | No ✗ |

9. If you are not recommending a Full Impact assessment please explain why.

Signature of policy developer / lead manager / director | Date of completion and submission

Names and signatures of members carrying out the Screening Assessment
1. Dan Thomas
2. Mike Wilcock

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead, c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

A summary of the results will be published on the Trust’s web site.

Signed _____ Dan Thomas and Mike Wilcock ___________

Date _______ June 2014 ___________