Management of Dementia in Primary Care

The shared care agreements for the acetylcholinesterase inhibitors (AChEI) and memantine, have been in place between primary and secondary care for over 10 years. The cost of AChEI and memantine has dropped due to the availability of generic versions of these drugs becoming available to the NHS. Due to this price drop and cost effectiveness, the practice of stopping AChEI at the severe stage of dementia has changed. The benefits of continuing treatment in a stable patient who is tolerating the medication outweighs the risk of stopping treatment with a catastrophic decline.

JAPC (with the endorsement of consultants at DTHFT) have decided to move away from the Shared Care Agreements for the dementia drugs based on the price drop, national consensus and growing experience in use of these drugs and now advocate the management of dementia in primary care after specialist initiation.

- Prescribing of acetylcholinesterase inhibitors (AChEI) and memantine are no longer under shared care.
- The diagnosis of dementia will only be made after a specialist assessment. Diagnosing the type of dementia is important in drug treatment choice.
- The initial role of primary care in the diagnosis of dementia is to offer a brief screen. There are some cognitive tools available for use in primary care. See appendix 2 for the general practitioners assessment of cognition. Further tools can be found at Dementia revealed – what primary care needs to know
- Only specialists in the care of patients with dementia should initiate treatment. The specialist will oversee the initial response to treatment usually with a 3 month review to assess for response. Specialist will identify those patients that can be safely managed in primary care and those requiring continued specialist service input.
- Patients should be stabilised on treatment before referral to primary care.
- Patients should only be referred back to the specialist if their cognitive behaviours changes and specialist support is required.
- There are no specific monitoring requirements for AChEI and memantine.
- There is little difference between AChEi except for cost and tolerability which are key factors in drug choice.
  - Donepezil is the preferred 1st line choice.
  - If two AChEI have been tried there is no point in trying another.
  - Memantine is an alternative to AChEI if cardiac adverse effects preclude their use.
- Before referral to specialist services, primary care should assess the patient’s anticholinergic burden. (See appendix 3)
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Introduction
JAPC has classified AChEIs (donepezil, rivastigmine, galantamine) and memantine as GREEN after specialist/consultant initiation. Patients will be stabilised on treatment before referral to primary care.

Specialist responsibilities:
- **Diagnosis**
  Specialist services will continue to diagnose, assess suitability and undertake appropriate baseline cognitive and functional assessments.
- **Initiation of treatment**
  The specialist will initiate treatment after careful consideration of the most appropriate drug, taking into account any contra-indications, cautions, side-effects, drug interactions, compliance issues and cost.
  - The specialist will undertake a 3 week review to assess side-effects and 3 month review to assess for response.
  - Stable patients will be discharged to the GP
  - Unstable patients to remain under the specialist for follow-up; this could include patient with mental health co-morbidities, tolerance problems or the need for specific risk management.
- **Dose increase**
  The specialist will assess the patient for tolerability to the treatment and titrated upwards as appropriate.

Discharge to GP:
- Patients will only be discharged to the GP once the patients care plan is stable or predictable. The patient will be given 4 weeks supply of maintenance treatment.
- The GP will continue drug treatment started by the specialist. The GP may withdraw or stop treatment if considered not to be worthwhile e.g. in extreme frailty.
- To be aware of common side effects and drug interactions. (see prescribing information p.5)
- The GP will stop treatment if the patient experiences nausea and vomiting, weight loss or tachycardia.
- **Monitoring**
  No special monitoring is required
  Annual dementia QOF review
  Usual review for new adverse reactions, drug interactions and compliance with treatment
- **Length of treatment**
  May be continued as long as it is well tolerated and administration burden is acceptable.
  In the event of a decision to stop treatment with AChEi, the dose should be reduced gradually to minimise the risk of discontinuation reaction such as increased agitation or disturbed sleep
- **Referral to specialist**
  Patients may be referred back for specialist review if their condition deteriorates or if any aspect of mental health care becomes concerning or where patient is no longer benefiting from treatment, and specialist support is necessary.

Prescribing note
1. Combination treatment of Memantine with an AChEI such as Donepezil, Rivastigmine or Galantamine is not a strategy supported by Derbyshire but they may be prescribed together short term when switching from AChEI to maintenance dose of Memantine.
2. **Aspirin and vascular dementia** - Low-dose aspirin can improve the prognosis of heart disease and stroke, possibly by reducing clot formation within the blood vessels and helping to maintain or improve blood flow to the heart and brain. Many doctors assume that aspirin will also provide some benefit for people with vascular dementia. A Cochrane review, 2012, shows that there is no evidence to suggest that aspirin is useful for people with vascular dementia. It is possible that vascular dementia and stroke are caused by different pathological processes. Practitioners need to be aware of the risks of aspirin, such as haemorrhages, which can be fatal.
3. **Statin and vascular dementia** - The current evidence that statins slowed progression in vascular dementia is inconclusive.
## Prescribing information

<table>
<thead>
<tr>
<th>1st line</th>
<th>2nd line</th>
<th>2nd line</th>
<th>2nd line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donepezil</strong></td>
<td><strong>Rivastigmine</strong></td>
<td><strong>Galantamine</strong></td>
<td><strong>Memantine</strong></td>
</tr>
<tr>
<td>Available as tabs and orodispersible tabs</td>
<td>Available as caps, solution and patch</td>
<td>Available as tabs, MR tabs and liquid</td>
<td>Available as tabs and solution</td>
</tr>
</tbody>
</table>

### Dose and route of administration

<table>
<thead>
<tr>
<th>Tablet</th>
<th>Capsule &amp; liquid</th>
<th>Tablet &amp; liquid</th>
<th>Oral tablets or solution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Starting dose:</strong></td>
<td><strong>Starting dose:</strong></td>
<td><strong>Starting dose:</strong></td>
<td>• Week 1: 5mg once daily (with or without food).</td>
</tr>
<tr>
<td>5mg in the evening</td>
<td>1.5mg twice daily with meals.</td>
<td>4mg twice daily preferably with meals.</td>
<td>• Week 2: 10mg once daily.</td>
</tr>
<tr>
<td><strong>Increasing to:</strong></td>
<td><strong>Increasing to:</strong></td>
<td><strong>Increase to:</strong></td>
<td>• Week 3: 15mg once daily.</td>
</tr>
<tr>
<td>10mg/day if tolerated after minimum 4 weeks</td>
<td>Maximum tolerated up to 6mg twice daily. Minimum of 2 weeks between dose increases.</td>
<td>Maximum tolerated up to 12mg twice daily. Minimum of 4 weeks between dose increases.</td>
<td>• Week 4 onwards: 20mg once daily.</td>
</tr>
</tbody>
</table>

Orodispersible tablet available

### Patch

**If oral preparations poorly tolerated/difficult to administer**

- Starting at: 4.6mg/24 hours
- Increasing to: 9.5mg/24 hours after a minimum of 4 weeks.

(Alzest is the cost-effective brand)

### Modified release tablet*

- 8mg once daily increasing to maximum tolerated up to 24mg once daily. Minimum of 4 weeks between dose increases.

("Luventa XL is the cost-effective brand")

### Prescribed indications

These medicines may be prescribed in Derbyshire in line with NICE Technology Appraisal 217 Alzheimer’s Disease:

For management of cognitive, non-cognitive, behavioral and psychological symptoms in people with Alzheimer’s Disease of mild to moderate severity (MMSE score 10-26 unless the MMSE is not an appropriate measure of cognition in individual cases).

NICE Clinical Guideline 42 Dementia:

- For relief from non-cognitive symptoms causing significant distress to the individual, or leading to behaviour that challenges in people with Lewy Body Dementia.
- For relief from non-cognitive symptoms and/or behaviour that challenges in people with Alzheimer’s Disease of any severity, causing significant distress or potential harm to the individual if
  - (a) a non-pharmacological approach is inappropriate or has been ineffective and
  - (b) other pharmacological options are inappropriate or have been ineffective (see also Derbyshire JAPC/DHCFT BPSD guidelines)

Memantine is only licensed in dementia of Alzheimer’s type classified as moderate to severe.

In Derbyshire, Memantine may be used for symptomatic treatment of moderate Alzheimer’s disease where AChEIs are contra-indicated or where at least two AChEI have not been tolerated.

Memantine monotherapy is an option for managing symptoms of severe Alzheimer’s disease.

Patients with Alzheimer’s disease already taking a AChEI, who then progress to severe dementia may be offered Memantine after phased withdrawal of AChEI if it is felt this would be of benefit in
### NICE Clinical Guideline 35 Parkinson’s Disease:
For managing cognitive and non-cognitive symptoms including psychosis in Dementia of Parkinson’s Disease, for which Rivastigmine is licensed.

For relief from severe non-cognitive behavioural and psychological symptoms of Alzheimer’s disease, Memantine or AChEI may be considered an option (within their respective licensed indications), where antipsychotics are inappropriate or are ineffective.

For relief of BPSD associated with Lewy Body Dementia and Parkinson’s Disease Dementia, Memantine is not licensed and is not to be used in Derbyshire. Consult local guidelines and NICE Clinical Guideline 42 Dementia.

### Renal/hepatic impairment

<table>
<thead>
<tr>
<th>Renal/hepatic impairment</th>
<th>No dosage adjustment in mild/moderate renal impairment.</th>
<th>Mild-moderate renal impairment may experience increased side-effects with Rivastigmine therefore advice to increase dose as tolerated should be closely observed.</th>
<th>Galantamine is contra-indicated in patients with severe renal or hepatic impairment.</th>
<th>Mild renal function (CrCl 50 – 80 ml/min) - no dose adjustment is required. Moderate renal impairment (CrCl 30 - 49 ml/min) - 10 mg/day. If tolerated well after at least 7 days of treatment, the dose could be increased up to 20 mg/day according to standard titration scheme. Severe renal impairment (CrCl 5 – 29 ml/min) - 10 mg/day</th>
</tr>
</thead>
</table>

### How long to treat
Treatment can be continued as long as it is tolerated and not a burden.

### When to consider stopping treatment
Treatment should be stopped in frail elderly, patients under end of life care if medication is not tolerated e.g. causing nausea, weight loss or bradycardia and in patients with anxiety or agitation.

### How to discontinue
If significant adverse effects are not a problem and if maintenance dose is greater than usual starting dose, it is preferable to gradually reduce dose before discontinuation to avoid possibility of discontinuation symptoms. Monitor closely and if there is a rapid and significant worsening of cognitive, functional or behavioural symptoms, consider the merits of restarting promptly as delay may reduce chance of a return to recent baseline functioning.

If significant adverse effects are not a problem, it is preferable to gradually reduce the dose before stopping, to avoid possible discontinuation symptoms.

### Adverse effects
Adverse reactions (e.g. hallucinations in Alzheimer’s Disease or worsening of extrapyramidal symptoms in those with Parkinson’s Disease Dementia) may respond to dose reduction or otherwise discontinuation. Depending upon the nature of adverse effects, a trial of a different AChEI may prove worthwhile.

Common: tiredness, confusion, dizziness, constipation, headache, dyspnoea, hypertension.
These medicines can cause bradycardia so **caution advised in patients with sick sinus syndrome or cardiac conduction deficits**. May cause increased gastric secretions so take care in patients with active ulcers or who are predisposed to these. Prescribe with care in patients with a history of asthma or COPD. For a full list of adverse effects and cautions see BNF and manufacturers’ summaries.

<table>
<thead>
<tr>
<th>Managing adverse effects</th>
<th>Adverse effect</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting or diarrhoea</td>
<td>Advise patient to take with or after food. Ensure plenty of fluids. May respond to dose reduction. Check compliance not intermittent (esp. Rivastigmine – see Dose section)</td>
<td>Less common: hallucinations, vomiting, anxiety, abnormal gait</td>
</tr>
<tr>
<td>Insomnia, abnormal dreams/nightmares, muscle cramps, fatigue</td>
<td>May respond to dose reduction</td>
<td>Rare: seizures (caution in epilepsy/history of convulsions), pancreatitis.</td>
</tr>
<tr>
<td>Syncope, dizziness</td>
<td>Consider bradycardia, heart block. Request ECG</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>Paracetamol if appropriate</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Monitoring requirements</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor for adverse effects noting that renal impairment or hepatic impairment may reduce an individual’s tolerability to Rivastigmine and/or Donepezil – see ‘Adverse Effects’ above and manufacturers’ summaries.</td>
<td>Monitor for adverse effects, especially if used in patients with poorly controlled hypertension, uncompensated congestive heart failure (NYHA III-IV) or who have had recent myocardial infarction. Seek specialist advice where necessary. Report any concerns regarding non-adherence to the specialist. Refer patient to mental health services in the event of deteriorating clinical condition.</td>
<td></td>
</tr>
<tr>
<td>Report any concerns regarding non-adherence (if remedial action cannot be taken in primary care) to the specialist.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refer patient to specialist in the event of deteriorating clinical condition, if any aspect of mental health care becomes concerning or where specialist support is necessary.</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
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</thead>
<tbody>
<tr>
<td>May interact with medicines that have anticholinergic activity e.g. oxybutynin. Potential for synergistic activity with medicines such as succinylcholine (suxamethonium) &amp; other neuromuscular blocking agents, cholinergic agonists or beta-blocking agents that have effects on cardiac conduction. Rivastigmine: Pharmacokinetic interactions unlikely</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil and galantamine: Both metabolised via CYP3A4 and CYP2D6 pathways in the liver. Inhibitors of these pathways (e.g. erythromycin, ketoconazole, fluvoxamine, fluoxetine, paroxetine) may increase drug levels and patients may experience increased side effects. A dose reduction may be required. Enzyme inducers (e.g. carbamazepine, phenytoin) may reduce drug levels and so such combinations should be used with care. See manufacturers’ summaries for full details.</td>
<td>Levodopa, dopaminergic agonists, anticholinergics and amantadine – memantine may enhance effects of these. Antipsychotics and barbiturates – memantine may reduce effect of these. Dantrolene and baclofen – memantine may alter effect of these. Avoid ketamine, dextromethorphan, amantadine – possible CNS toxicity. Ranitidine, cimetidine, quinine, quindine, procainamide and nicotine - plasma level of these and/or memantine may be increased.</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 1 - PROCESS FOR IDENTIFYING AND MANAGING DEMENTIA IN DERBYSHIRE NHS ORGANISATIONS.
(Kindly adapted from Nottinghamshire APC)

PATIENT PRESENTS IN PRIMARY CARE WITH COGNITIVE IMPAIRMENT

INVESTIGATIONS AND ASSESSMENTS TO SUPPORT DIAGNOSIS
- Take history and review medication (see anticholinergic burden drugs in appendix 3)
- Cognitive and mental state examination – GPCOG/6-CIT/MOCA if appropriate for patient
- Physical examination including basic neurological and cardiovascular examination plus check:
  | U&Es, Calcium, eGFR, Glucose, LFTs | FBC, ESR, B12 & Folate | TFTs |
- Consider ECG if being co-prescribed with medicinal products that have the potential to cause torsades de pointes or the patient has an existing cardiac condition, cardiovascular problems are known or suspected or family history.

OFFER REFERRAL TO SPECIALIST SERVICES (mental health/neurology) for assessment & diagnosis

Health & social care professionals provide information
- Signs & symptoms
- Course & prognosis
- Treatments
- Local care & support services
- Support groups
- Sources of financial & legal advice & advocacy
- Medico-legal issues including driving, LPA
- Local information, e.g. libraries, volunteer orgs.

TREATMENT FOR COGNITIVE SYMPTOMS
- Non-pharmacological NICE Guideline CG42
- Pharmacological Acetylcholinesterase Inhibitors, Memantine, NHS England Pragmatic Resource for GPs

MANAGEMENT OF ANY BEHAVIOURAL OR PSYCHOLOGICAL SYMPTOMS (BPSD)

INTEGRATED HEALTH & SOCIAL CARE PLAN
Carer referred for assessment where appropriate

PATIENT DISCHARGED TO GP once stable
- Prescribe specialist-initiated medication
- Annual dementia QOF review
- No specific extra monitoring
- Usual review for new adverse reactions, drug interactions and compliance with treatment

REFER TO SPECIALIST SERVICES AS REQUIRED
See contacts under communications and support

Patient stable

Patient becomes unstable
If BPSD arise undertake assessment to exclude delirium/establish likely causes (BPSD guideline)

- AChEIs are licensed for mild to moderate dementia but in practice may be helpful continued into severe dementia
- If GP decides to stop AChEI or Memantine treatment e.g. in extreme frailty, and maintenance dose is greater than starting dose, ideally taper dose (by 1/3 to ½ over 2 to 4 weeks) to minimise risk of discontinuation reaction such as increased agitation or disturbed sleep.
  E.g. Rivastigmine 4.5mg BD → 3mg BD for 2 weeks → 1.5mg BD for 2 weeks → stop
  Donepezil 10mg OD → 5mg OD for 4 weeks → stop
- Consider re-starting treatment promptly if marked deterioration occurs upon stopping
- Memantine is licensed for moderate or severe Alzheimer’s and may be continued long term if deemed helpful
- Combination treatment with AChEI & Memantine is not a strategy supported by Derbyshire but may be prescribed together short term when switching from AChEI to maintenance dose of Memantine

Produced: February 2017
Review date: January 2019
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Appendix 2 - GENERAL PRACTITIONER ASSESSMENT OF COGNITION (GPCOG)

GPCOG Patient Examination
Unless specified, each question should only be asked once

Name and address for subsequent recall
"I am going to give you a name and address. After I have said it, I want you to repeat it. Remember this name and address because I am going to ask you to tell it to me again in a few minutes: John Brown, 42 West Street, Kensington"

(Allow a maximum of 4 attempts but do not score yet)

Time Orientation
What is the date? (Accept exact only)
0 points—incorrect
1 point—correct

Clock drawing (visuospatial functioning) use a paper with a printed circle.
Please mark in all the numbers to indicate the hours of a clock (Correct spacing required).

For a correct response (above), the numbers 12, 3, 6, and 9 should be in the correct quadrants of the circle and the other numbers should be approximately correctly placed.

Please mark in hands to show 10 minutes past eleven o'clock (11:10).
For a correct response (above), the hands should be pointing to the 11 and the 2 but do not penalise if the respondent fails to distinguish the long and short hands.

Information
Can you tell me something that happened in the news recently? (Recently = in the last week)
Respondents are not required to provide extensive details, as long as they demonstrate awareness of a recent news story.
If a general answer is given, such as "war", "a lot of rain", ask for details.
If unable to give details, the answer should be scored as incorrect.

Recall
What was the name and address I asked you to remember?
Score for each of the 5 components - John, Brown, 42, West Street, Kensington.

John 0 points—incorrect / 1 point—correct
Brown 0 points—incorrect / 1 point—correct
42 0 points—incorrect / 1 point—correct
West Street 0 points—incorrect / 1 point—correct
Kensington 0 points—incorrect / 1 point—correct

GPCOG Patient Score= /9

Appendix 3 - Anticholinergics and other drugs to be used with caution in dementia.

<table>
<thead>
<tr>
<th>Drugs for bladder instability</th>
<th>Avoid if possible. If not solifenacn is preferred to tolerodine or oxybutynin.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiemetics</td>
<td>Domperidone and ondansetron preferred to cyclizine, metoclopramide, prochlorperazine (and other phenothiazines).</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Avoid if possible. If not, loratadine and fexofenadine are preferred to chlorpheniramine, promethazine and hydroxyzine.</td>
</tr>
<tr>
<td>Tricyclics generally</td>
<td>Includes the very commonly used amitriptyline.</td>
</tr>
<tr>
<td>Analgesics</td>
<td>Avoid tramadol and pethidine in particular.</td>
</tr>
<tr>
<td>Sedation</td>
<td>All sedation to be used with caution - long acting benzodiazepines and anti-psychotics especially.</td>
</tr>
</tbody>
</table>

Further resources for GPs

Further resources for patients
- Alzheimer’s society (factsheets are available) 0845 300 0336 or [www.alzheimers.org.uk](http://www.alzheimers.org.uk)
- Patient UK: [www.patient.co.uk](http://www.patient.co.uk)
- Dementia UK ([www.dementiauk.org](http://www.dementiauk.org)
- NHS Choices ([www.nhs.uk](http://www.nhs.uk)
- Choice and Medication: [Derbyshire Healthcare NHS Foundation Trust: choice and Medication](http://www.derbyshirehealthcareft.nhs.uk/)

Communication and support
Consultant psychiatrist to whom the patient is known or duty consultant via switchboard:
- South: 01332 623700 (24h)
- North: 01246 515964
- High Peak: 01298 24149

Kingsway Hospital Pharmacy Department: 01332 623700 ext 33495 or 33268

Consultant Psychiatrist

<table>
<thead>
<tr>
<th>Dementia Care Neighbourhood Team</th>
<th>Consultant</th>
<th>Contact Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erewash</td>
<td>Dr Christine Taylor</td>
<td>Ilkeston Resource Centre 0300 123375</td>
</tr>
<tr>
<td>Ambergale</td>
<td>Dr Fairooz Hassiem</td>
<td>Ripley Library 0300 123 2673</td>
</tr>
<tr>
<td>Derby City</td>
<td>Dr Parker</td>
<td>St Andrews House 0300 123 4011</td>
</tr>
<tr>
<td></td>
<td>Dr Prakash</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dr Raisi</td>
<td></td>
</tr>
<tr>
<td>South Derbyshire &amp; South Dales</td>
<td>Dr Hartman</td>
<td>Dalebank View 0300 123 3376</td>
</tr>
<tr>
<td>Chesterfield</td>
<td>Dr Sykes</td>
<td>Walton Hospital 01246 515971 Corbar View 03001 233374 Walton Hospital 01246 515725</td>
</tr>
<tr>
<td>High Peak &amp; North Dales</td>
<td>Dr Mayo</td>
<td>Dr Whittingham</td>
</tr>
<tr>
<td>Bolsover &amp; Clay Cross</td>
<td>Dr Whittingham</td>
<td>0300 123 3371</td>
</tr>
<tr>
<td>Killamarsh &amp; North Chesterfield</td>
<td>Dr Saxena</td>
<td>0300 123 3370</td>
</tr>
</tbody>
</table>