DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Medication and Prescribing in the Management of Dementia in Primary Care

In 2017 JAPC (with the endorsement of consultants at DHCFT) decided to move away from 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.

- The initial role of primary care in the diagnosis of dementia is to offer a brief screen. There are several cognitive assessment tools available for use in primary care. See appendix 3 General practitioner assessment of cognition (GPCOG) as an example. Other tools can be found in Dementia revealed – what primary care needs to know document- in appendix 3 (p.39-44) useful scales. The diagnosis of dementia will only follow referral to a specialist and is be made after a specialist assessment. Diagnosing the type of dementia is important in drug treatment choice.

- Assess anticholinergic burden using validated tools at initial screening (before referral to specialist services) and at medication reviews with people living with dementia. Examples include Anticholinergic Cognitive Burden (ACB) scale and Modified anticholinergic risk scales (mARS) scale.

- Specialists in the care of patients with dementia will 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.

- Seek advice from the specialist if behavioural and psychological symptoms or risks emerge and specialist support is required.

- There are no specific monitoring requirements for AChEI and memantine. If annual health check identifies deteriorating renal function be aware the maximum recommended dose for memantine is 10mg when CrCl < 30 ml/min.

- 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.

- Case finding in primary care is not recommended due to lack of evidence of benefit and possibility of 'false positive' diagnosis leading to inappropriate treatment and unnecessary stress.

- JAPC has classified AChEIs (donepezil, rivastigmine, galantamine) and memantine as below:
    - **GREEN** after specialist/consultant initiation for newly diagnosed patients.
    - **GREEN** for patients with BPSD (see separate guideline)
    - Memantine is **GREEN** as add on to an AChE inhibitor in patients with established Alzheimer's disease. This can be started on specialist recommendation or by GP. Advice about the appropriateness of adding in memantine is available from the specialist if needed through advice & guidance request.

Specialist responsibilities:

- **Diagnosis**
  Specialist services will continue to diagnose, assess suitability and undertake appropriate baseline cognitive and functional assessments.
- **Initiation of treatment for newly diagnosed patients**
  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.

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.
- To be aware of common side effects and drug interactions. (see prescribing info appendix 2)
- The GP will stop treatment if the patient experiences nausea and vomiting, weight loss or bradycardia.
- **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.
  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.

  The GP may withdraw or stop treatment if considered not to be worthwhile e.g. in extreme frailty.
  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

  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. e.g. Donepezil 10mg OD → 5mg OD for 4 weeks → stop; Rivastigmine 4.5mg BD → 3mg BD for 2 weeks → 1.5mg BD for 2weeks → stop
- **Referral to specialist**
  Seek advice or refer back for specialist review if any aspect of mental health care becomes concerning or where specialist support is necessary.

Prescribing note

1. **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.
2. **Statin and vascular dementia**- The current evidence that statins slowed progression in vascular dementia is **inconclusive**.

NICE NG97 recommendations- Do NOT offer aspirin/ statin to slow the progress of Alzheimer's disease, except as part of a randomised controlled trial

NICE Guideline [NG97] Dementia: assessment, management and support for people living with dementia and their carers. NICE, June 2018

British National Formulary: https://bnf.nice.org.uk/treatment-summary/dementia.html

Brief summary of pharmacological management of dementia as recommended by NICE NG 97

Pharmacological management of Alzheimer's disease (1.5.2 – 1.5.9) • **Acetylcholinesterase inhibitors** (AChEIs) as monotherapies are recommended options for manging mild to moderate Alzheimer's disease (AD). • **Memantine** monotherapy is recommended as an option for managing AD for people with moderate AD who are intolerant of or have a contraindication to AChEIs or who have severe AD. • For people who are not taking an AChEI or memantine, prescribers should only **start treatment** on the advice of a clinician who has the necessary knowledge and skills. Once a decision has been made to start an AChEI the first prescription **may** be made in primary care. • For people with an **established diagnosis** of AD who are already taking an AChEI, memantine can be **considered** if they have moderate AD and **offered** if they have severe AD; primary care prescribers may start treatment without taking advice from a specialist clinician. • Do not stop AChE inhibitors in people with Alzheimer's disease because of disease severity alone	NG97, section 1.5
Pharmacological management of non-Alzheimer's dementia (1.5.10 – 1.5.17) (NB: NICE recommendations include off-label use of medicines) **Dementia with Lewy Bodies (DLB):** • **Offer** donepezil or rivastigmine to people with mild or moderate DLB • Only **consider** galantamine for people with mild to moderate DLB if donepezil and rivastigmine are not tolerated • **Consider** memantine for people with DLB if AChEIs are not tolerated or are contraindicated **Parkinson's Disease Dementia (PDD)** • For guidance on the pharmacological management of PDD see the NICE guideline on Parkinson's Disease **Vascular dementia** • Only **consider** AChEIs or memantine for people with vascular dementia of they have suspected comorbid AD, PDD or DLB **Frontotemporal dementia (FTD)** • **Do not offer** AChEIs or memantine to people with FTD	NG97, section 1.5
Medicines that may cause cognitive impairment (1.6) Be aware that some commonly prescribed medicines are associated with increased anticholinergic burden and therefore cognitive impairment. There are validated tools for assessing anticholinergic burden but there is insufficient evidence to recommend one over the others.	NG97, section 1.6 Anticholinergic Burden Calculator (ADBCalc) Modified Anticholinergic Risk Scale (mARS)
Managing non-cognitive symptoms (1.7) Before starting non-pharmacological or pharmacological treatment for distress in people living with dementia conduct a structured assessment to explore possible	NG97, section 1.7 DHCFT/JAPC BPSD guidelines

reasons for their distress and to check for and address clinical or environmental causes (for example pain, delirium or inappropriate care)	

List of pharmacological interventions not recommended by NICE in NG97

- 1.4.6 Do not offer ginseng, vitamin E supplements or herbal formulations to treat dementia
- 1.5.5 Do not stop AChEIs in people with Alzheimer's disease because of disease severity alone
- 1.5.15 Do not offer AChEIs or memantine to people with frontotemporal dementia
- 1.5.16 Do not offer AChEIs or memantine to people with cognitive impairment caused by multiple sclerosis
- 1.7.10 Do not offer valproate to manage agitation or aggression in people living with dementia unless it is indicated for another condition
- 1.7.12 Do not routinely offer antidepressants to manage mild to moderate depression in people living with mild to moderate dementia, unless they are indicated for a pre-existing severe mental health problem
- 1.7.13 Do not offer melatonin to manage insomnia in people living with Alzheimer's disease
- 1.10.8 Do not routinely use enteral feeding in people living with severe dementia unless indicated for a potentially reversible comorbidity
- 1.5.9 Do not offer the following specifically to slow the progress of Alzheimer's disease, except as part of a randomised controlled trial: Diabetes or Hypertension medicines; Statins; NSAIDs including aspirin

Additional resources

Dementia diagnosis and management: A brief pragmatic resource for general practitioners. NHSE, January 2015 dementia-diag-mng-ab-pt.pdf (england.nhs.uk)

Dementia Revealed: What primary care needs to know. NHSE, November 2014 dementia-revealed-toolkit.pdf (england.nhs.uk)

Dementia – manging behavioural and psychological symptoms in people with dementia DHCFT/JAPC BPSD guidelines

Choice and Medication https://www.choiceandmedication.org/derbyshcft

Credible Meds - Online resource for information on medicines that prolong QTc interval or cause Torsades de Pointes https://www.crediblemeds.org/ (free registration required)

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

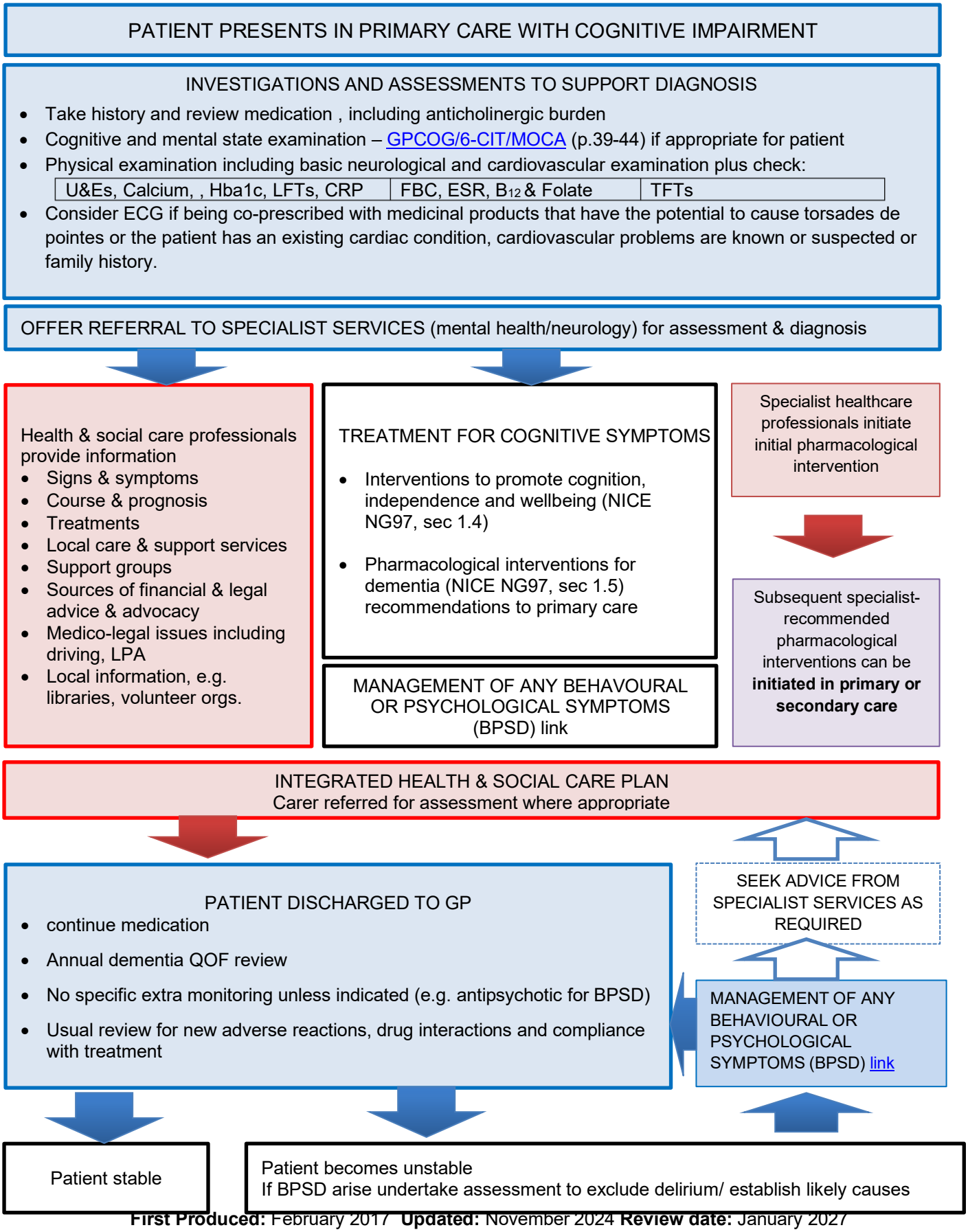
DHCFT Kingsway Hospital Pharmacy Department: 01332 623700 extension 33268

Consultant Psychiatrist

Dementia Care Neighbourhood Team	Consultant	Contact Details
Erewash	Dr Nisha Mokashi	Ilkeston Resource Centre 0300 123375
Amber Valley	Dr Zarar Ahmed	Ripley Library 0300 123 2673
Derby City	Dr Parker	St Andrews House 0300 123 4011
	Dr Prakash	
	Dr Raisi	
South Derbyshire & South Dales	Dr Farrington	Dalebank View 0300 123 3376
Chesterfield	Dr Cosmulescu	Walton Hospital 01246 515971
High Peak & North Dales	Dr Mayo	Corbar View 03001 233374
	Dr John Sykes	Walton Hospital 01246 515725
Bolsover & Clay Cross	Dr Burton	0300 123 3371

Killamarsh & North Chesterfield	Dr Saxena	0300 123 3370

Appendix 1 - PROCESS FOR IDENTIFYING AND MANAGING DEMENTIA IN DERBYSHIRE NHS ORGANISATIONS.
(Kindly adapted from Nottinghamshire APC, updated Dec 2021)



Appendix 2 Prescribing information

Drug	Donepezil	Rivastigmine	Galantamine	Memantine
Formulations	Available as tabs and orodispersible tabs	Available as caps, solution and patch	Available as MR tabs and solution	Available as tabs, orodispersible tabs and solution
Place in therapy	**1st line**	**2nd line**	**2nd line**	**2nd line**
Dose and route of administration (annual cost as per Drug Tariff September 2024)	**Tablet** Starting dose: • 5mg in the evening (£22) Increasing to: • 10mg/day if tolerated after minimum 4 weeks (£16) Orodispersible tablet available but more expensive (£1287)	**Capsule** Starting dose: • 1.5mg **twice daily** with meals. Increasing to: • Maximum tolerated up to 6mg (2x3mg) (£34) twice daily. Minimum of 2 weeks between dose increases. **Oral solution** 2mg/ml oral solution SF available but expensive (520 at 4mg BD) **Patch** (preferred brand **Alzest**) If oral preparations poorly tolerated/difficult to administer Starting at: • 4.6mg/24 hours (£936) Increasing to: • 9.5mg/24 hours after a minimum of 4 weeks (£298) • increase if necessary to 13.3 mg/24 hours daily after 6 months (£936) See BNF for dose equivalence and conversion Zeyzelf 4.6mg/24hrs & 9.5mg/24hrs patches are to be applied **TWICE** weekly.	**Modified release tablet** (Preferred brand **Luventa XL)** Starting dose: 8mg once daily (£622) increasing to maximum tolerated up to 24mg once daily (£915). Minimum of 4 weeks between dose increases. **Oral solution** 20mg/5ml oral solution SF very expensive (£2640 at 12mg BD)	**Tablets** (take with or without food). • Week1: 5mg once daily • Week 2: 10mg once daily. • Week 3: 15mg once daily. • Week 4 onwards: 20mg once daily (£18) 20mg Orodispersible SF tablets (£600) available but more expensive **Oral solution** 10mg/ml oral solution SF available (20mg once daily: £286)

<table>
<tr><td>Renal/hepatic impairment</td><td>No dosage adjustment in mild/moderate renal impairment.

Patients with mild to moderate hepatic impairment may experience increased side-effects with donepezil therefore advice to increase dose as tolerated should be closely observed</td><td>Mild-moderate renal impairment may experience increased side-effects with Rivastigmine therefore advice to increase dose as tolerated; should be closely observed.

Patients with mild to moderate hepatic impairment may experience increased side-effects with rivastigmine therefore advice to increase dose as tolerated should be closely observed</td><td>Galantamine is contra-indicated in patients with severe renal or hepatic impairment.</td><td>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

No dose adjustment needed in mild or moderate hepatic impairment</td></tr>
<tr><td>Adverse effects</td><td colspan="3">• 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.
• These medicines can cause bradycardia so caution advised in patients with sick sinus syndrome or cardiac conduction deficits.
• May cause increased gastric secretions- take care in patients with active ulcer or who are predisposed to it
• 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.</td><td>• Common: tiredness, confusion, dizziness, constipation, headache, dyspnoea, hypertension.
• Less common: hallucinations, vomiting , anxiety, abnormal gait
• Rare: seizures (caution in epilepsy /history of convulsions), pancreatitis.</td></tr>
<tr><td>Managing adverse effects</td><td colspan="3"><table>
<tr><th>Adverse effect</th><th>Action</th></tr>
<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></tr>
<tr><td>Insomnia, abnormal dreams/nightmares, muscle cramps, fatigue</td><td>May respond to dose reduction</td></tr>
<tr><td>Syncope, dizziness</td><td>Consider bradycardia, heart block. Request ECG</td></tr>
<tr><td>Headache</td><td>Paracetamol if appropriate</td></tr>
</table></td><td>Tiredness, dizziness, abnormal gait or hypertension may respond to dose reduction</td></tr>
</table>

Drug interactions	May interact with medicines that have anticholinergic activity e.g. oxybutynin. Potential for synergistic activity with medicines such as succinylcholine (suxamethonium) & other neuromuscular blocking agents, cholinergic agonists or beta-blocking agents that have effects on cardiac conduction. Rivastigmine: Pharmacokinetic interactions unlikely 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.	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, quinidine, procainamide and nicotine - plasma level of these and/or memantine may be increased.

Document Control

Amendment	**Date**
Page 1 – Memantine with renal impairment. Renal function terminology changed from eGFR to CrCl for consistency	February 2025

Appendix 3 - GENERAL PRACTITIONER ASSESSMENT OF COGNITION (GPCOG)

NICE NG57- GPCOG test is used to screen for dementia and no published evidence was found in a population with suspected dementia (the available studies were all on dementia screening). Other examples of validated brief structured cognitive instruments includes the 6-item cognitive impairment test (6CIT) and Test Your Memory (TYM).

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

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).

0 points - incorrect 1 point - correct

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).

0 points - incorrect 1 point - correct

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)

0 points - incorrect 1 point - correct

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

GPCOG: The General Practitioner Assessment of Cognition www.gpcog.com.au/