Dementa Formulary Guidance [v1.0]

1. Introduction

These Guidelines are intended for routine use. However there will be instances where they are not suitable for the patient you are managing, where more bespoke treatment will be necessary. In such instances the rationale for prescribing away from formulary must be recorded.

2. Pharmacological treatments in dementia – Key Points

- The three acetylcholinesterase (AChE) inhibitors (donepezil, galantamine and rivastigmine) are recommended options for mild to moderare Alzheimers disease.
- Memantine is an option for moderate Alzheimer's disease in people who are intolerant of or have a contraindication to AChE inhibitors or for severe Alzheimers disease. They should only be initiated by specialists in dementia care.
- The treatment should be continued in primary care under the area specific shared care protocols. Once stabilised paatients must be reviewed at least annually, or more frequently if clinically indicated.
- Any relevant physical, sensory or learning disabilities, or communication difficulties should be considered to ensure equality of access to treatment for service users from different ethnic groups, and cultural backgrounds.
- Prescribers should discuss treatment options, benefits and risks with the service user and/or carer and seek carers views on the patients condition at baseline.
- If prescribing an AChE inhibitor, treatment should normally be started with a drug with the lowest acquisition cost, allowing for different formulations, taking into account adherence, medical co-morbidity, drug interactions and dosing profiles.
- When using pharmacological treatments in dementia, low initial doses and gradual dose increments are necessary.
- Monitor closely for any adverse drug reactions and review treatment if side effects are severe or intolerable. For further information see relevant SPC
- Carer views on the service user's condition at follow up should be considered.

3. Investigations and screening

Investigations are usually done in primary care, for suspected dementia. They include:

- Full blood count,
- ESR,
- urea and electrolytes,
- calcium,
- glucose,
- Liver function tests,
- thyroid function tests;
- serum vitamin B12/folate levels
- and iron studies, if indicated
- midstream urine culture to rule out UTI
- chest x-ray
- brain imaging
- ECG —if cardiovascular problems suspected or starting an AChEI

4. Continuation Criteria

Service users who continue on pharmacological treatments for dementia should be reviewed regularly using cognitive, global, functional and behavioural assessment. The treatment should be reviewed regularly, at least annually by specialist teams. Criteria for continuing therapy are

- Improvement / stabilization of cognitive function better than expected natural decline e.g. lees than expected decline in MMSE score of >5 points in 12 months in moderate disease or 5 points on the SIB over 6 months in severe disease.
- Meaningful improvement/ stabilization of functional ability as evidenced by improvement, stabilization or reduction in expected decline (<10/60 in 12 months) on clinically relevant items or total score on the BADL in moderate disease or improvement or stabilization in severe disease.
- Reduction in aggressive behaviour that challenges and/or psychosis as evidenced by NPI improved score of 2 or more in the relevant subscale over 6 months.
- An overall clinical global impression of stabilization or improvement must be stated.

5. Discontinuation Criteria

Discontinuation must be discussed first with the carers, family, and with the patient wherever possible. Discontinuing therapy should be considered when

- Adverse reaction to the medication
- Lack of compliance with the medication lack of evidence of efficacy i.e. the patient does not fulfil the criteria for continuation stated above
- Patient is on an end of life care pathway, staging equivalent to late amber/red of the Liverpool pathway
- If the treatment is for cognitive problems predominantly an MMSE of <5/30 or SIB score of <30/100
- An irreversible deterioration in the patients global clinical presentation since the last review e.g., a CVA
- An overall clinical global impression must state the treatment is no longer effective

6. Other Dementias

- While there is limited evidence for treatment with these agents for non-Alzheimer's dementias, NICE
  dementia guidance advises that if the underlying neurochemical deficit is similar, irrespective of the aetiology of the impairment, then it is possible that AChEI's or Memantine would produce a similar symptomatic effect in other types of dementia.
- Do not use acetylcholinesterase inhibitors in mild cognitive impairment. The potential benefits are unlikely to outweigh the increased risks of adverse effects
- NICE does not recommend the routine use of cholinesterase inhibitors or memantine for cognitive decline in vascular dementia.
- Mixed dementia should be managed according to what is considered the predominant cause of their dementia.
- Avoid use of antipsychotics in people with Parkinsons Disease dementia (PDD) or Dementia with Lewy Bodies (DLB) wherever possible, consider quetiapine or clozapine if necessary.

7. Behavioural and Psychological Symptoms of Dementia (BPSD)

Behavioural and psychological symptoms of dementia include a range of non-cognitive symptoms, such as apathy, anxiety, depression, agitation, aggression, delusions and hallucinations, wandering, incontinence, altered eating habits, sexual disinhibition, shouting, hoarding, repeated questioning and sleep disturbances.
Antipsychotics can be used for some severe symptoms of BPSD, however benefits are limited and they are asociated with an increased risk of stroke and mortality, along with other serious adverse effects such as sedation, EPSE, dehydration, falls, chest infections, and acclerated cognitive decline. Prescribing of these agents should be by specialist staff only.

The management of BPSD is discussed further below. Also see RDASH Protocol for Managing Behavioural and Psychological Symptoms in Patients with Dementia.

Table 1: ALZHEIMER'S DISEASE – PHARMACOLOGICAL TREATMENTS

First Line:	Relative Cost	Notes
(AChEI) Donepezil	£	Only dementia specialists in consultation with service user/carer should initiate treatment. Appropriate AChEI should be selected following consideration of cost, adverse effects, drug interactions, other conditions, expectations around concordance, and dosing profiles. Switching between agents may considered in cases of non-response or intolerance Continue AChEI only if benefits on cognitive, global, functional and behavioural symptoms.
Donepezil Orodispersible tablets	£	Both 5mg and 10mg are effective doses. Orodispersible tablets available Elimination half-life is long at about 70 hours
Galantamine (Oral solution)	££ (£££)	Oral solution and modified release preparations are available. Reductions in dose may be necessary in hepatic or renal impairment
Rivastigmine (Liquid) [Patches]	£ (££££) [£££]	Oral solution and patch also available; also licenced for mild to moderately severe dementia in idiopathic Parkinson's disease; Gastrointestinal side effects appear more frequent with rivastigmine. Patch may be appropriate in those unable to tolerate side effects of oral rivastigmine but application site reactions (erythema, pruritus, rash, vesicles) can occur
Second Line:	**Relative Cost**	**Notes**
Alternative AChEI Galantamine Rivastigmine	 ££ £££	If initial AChEI not tolerated or not effective, switch to another AChEI not already tried.
Memantine (Liquid)	££ (£££)	Recommended for moderate Alzheimer's disease in people who are intolerant of or have a contraindication to AChEIs or in severe Alzheimer's disease Only specialists in the care of people with dementia (in consultation with service user/carer) should initiate treatment.
Not Recommended	**Relative Cost**	**Notes**
Vitamin E Ginkgo biloba		Limited data available - difficult to determine evidence of clinical benefit
Memantine + AChEI	££-££££	Evidence of additional clinical efficacy is not clear. Written requests will be considered on a case by case basis by the Chief Pharmacist, Chair of Drugs & Therapeutics.??? Monitoring and continual review of clinical benefit essential.

Table 2: OTHER DIMENTIAS – PHARMACOLOGICAL TREATMENTS

Mild Cognitive Impairment	Relative Cost	Notes
AChEIs	£-££££	Do not use acetylcholinesterase inhibitors for mild cognitive impairment because any potential benefits are unlikely to outweigh the increased risk of side effects
Vascular Dementia	**Relative Cost**	**Notes**
AChEIs Memantine	£-££££ ££-££££	AChEIs and memantine are not licensed for the treatment of vascular dementia and should not be routinely prescribed for cognitive decline in vascular dementia Specialists may carefully consider exceptional use on a case-by-case basis (off-label use).
DLB or PDD	**Relative Cost**	**Notes**
AChEIs (Rivastigmine licensed for PDD) Memantine	£-££££ ££-££££	• Further studies are needed to establish the role of AChEIs and memantine • Use of AChE inhibitors may be considered in Parkinson's Disease Dementia (PDD) or dementia with Lewy Bodies (DLB) on a case-by-case basis. • Rivastigmine is the only AChEI licensed for symptomatic treatment of mild to moderately severe dementia in idiopathic Parkinson's disease • Memantine has not been widely investigated for use in DLB
Mixed Dementia	**Relative Cost**	**Notes**
AChEIs Memantine	£-££££ ££-££££	• NICE advises that people with mixed dementia should be managed according to what is considered the predominant cause of their dementia.

Table 3: PHARMACOLOGICAL MANAGEMENT OF BPSD

3a: Managing BPSD in Alzheimer's Disease

Key Symptom	First Line	Evidence Type	Second Line	Evidence Type
Depression	Sertraline Citalopram Mirtazapine (with sleep & appetite disturbance)	2 – 3 + £		
Apathy	Sertraline Citalopram	2-3 + £	AChEI[S]	2
Psychosis	Risperidone	1	Olanzapine, Aripiprazole; Memantine[S]	2
Severe physical aggression which is harmful to self or others	Risperidone[L] Haloperidol	1 2	Olanzapine, Aripriprazole, Lorazepam, Memantine[S]	2
Agitation/Anxiety	Citalopram	3	Lorazepam, Mirtazapine	2-4
Poor Sleep	Temazepam Zopiclone	3 +£	Zolpidem	3
Evidence Levels: 1= metanalysis, 2= RPCTs, 3= Other studies, 4= Expert opinion, £= cost implications Other superscript: L= licenced indication, S= secondary care initiation				

3b: Managing BPSD in Lewy Bodies or Parkinson's Disease Dementia

Key Symptom	First Line	Evidence Type	Second Line	Evidence Type
Depression	Citalopram	4 + £	Sertraline	4
Apathy	Sertraline Citalopram	4 +£	AChEI[S]	2
Psychosis*	Rivastigmine	2-3	Quetiapine[S], Donepezil[S], Galantamine[S]	3
Severe physical aggression which is harmful to self or others	Quetiapine	3	AChEI[S], Lorazapam	3-4
Moderate Agitation/ Anxiety	Citalopram	3+£	AChEI[S], Lorazepam	2-4
Poor Sleep	Temazepam, Zopiclone	3 +£	Zolpidem	3
REM sleep behaviour (nightmares, hyperactivity)	Clonzepam**	3		
Evidence Levels: 1= metanalysis, 2= RPCTs, 3= Other studies, 4= Expert opinion, £= cost implications Other superscript: L= licenced indication, S= secondary care initiation, *= consider reducing antiparkison's medication first, **= 500-1000mg nocte				

3c: RECOMMENDED DOSED FOR USE IN BPSD

Drug	Starting Dose	Maximum Dose
Risperidone	500 micrograms daily	1 mg BD
Olanzapine	2.5 mg daily	10 mg daily
Quetiapine	25mg daily	25 – 300 mg daily
Aripiprazole	5 mg daily	10 mg daily
Haloperidol	500 micrograms – 1 mg BD – TDS Oral/IM	1 mg TDS Oral/IM
Lorazepam	500 micrograms – 1 mg BD Oral/IM	1 mg QDS Oral/IM
Start at the minimum recommended dose and titrate according to response (usually every 2-4 days) to maximum tolerated dose. Consider cautious withdrawal after 6 weeks. Monitoring of antipsychotics should be in line with SPC and Schizophrenia Formulary Guidance		

3d: PHARMACOLOGICAL MANAGEMENT OF BPSD – OTHER INFORMATION

Drug Group	Relative Cost	Notes
Donepezil **Galantamine** **Rivastigmine**		AChEIs may have a beneficial effect on behavioural and psychological symptoms of dementia if symptoms are causing severe distress or leading to challenging behaviour. NICE advises that the following can be considered for an acetylcholinesterase inhibitor: • people with DLB who have non-cognitive symptoms causing significant distress or leading to behaviour that challenges or • 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: a non-pharmacological approach is inappropriate or has been ineffective, and antipsychotic drugs are inappropriate or have been ineffective • AChEIs should not routinely be used for non-cognitive symptoms or behaviour that challenges in vascular dementia
Memantine		The evidence for memantine for severe agitation is still developing however it may be beneficial in people with moderate to severe behavioural symptoms (agitation, aggression and/or psychotic symptoms) where: • non-pharmacological interventions are ineffective or inappropriate • where the severity of risk does not require use of antipsychotic medication • where treatment with antipsychotics is not tolerated or contraindicated • where longer term management is required
Mood stabilisers		Limited evidence; Low doses of carbamazepine (200mg/day – max 600mg) can be tried as a controlled therapeutic trial if other measures are ineffective. Carbamazepine may improve agitation and aggression but be aware of the risk of side effects and drug interactions; Routine use not recommended
Benzodiazepines e.g. Lorazepam; diazepam, clonazepam		Not routinely recommended except for short-term/PRN use only in severe cases when anxiety or agitation is prominent and other approaches have failed. Adverse effects can include dependence, tolerance, sedation, worsening cognition, delirium, increased risk of falls, disinhibiting effects and in some cases, respiratory depression or worsening of breathing disorders