Donepezil *(Aricept®)* (TLS status Amber in Swindon)

for the symptomatic treatment of mild to moderately severe Alzheimer's disease

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines how responsibility for prescribing donepezil for the symptomatic treatment of mild to moderately severe Alzheimer's disease, might be shared between specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

Donepezil is recommended as a treatment option for managing mild to moderate Alzheimer's disease. Treatment with donepezil should be initiated and stabilised within secondary care. Once the patients condition is clinically stable and assessed by specialists in dementia as benefiting from treatment, it can be appropriate for GPs/NMP to resume prescribing in accordance with this Shared Care Agreement (SCA).

Drug treatment for Alzheimer's disease should form part of a wider package of support and information for the patient and their carer. Treatment with donepezil should only be initiated if reasonable steps are taken to ensure adequate compliance.

This shared care is intended to apply to patients who have been initiated on treatment (and who have been assessed as benefiting) by a specialist in the care of patients with dementia, in accordance with the guidance from the NICE Technology Appraisal 'Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease' (NICE TA 217) and NICE Dementia Clinical Guideline 42. Specialists mainly include Old Age Psychiatrists but also Geriatricians and Neurologists.

The doctor who prescribes this medication legally assumes clinical responsibility for donepezil and the consequences of its use.

RESPONSIBILITIES and ROLES (insert as much additional text as appropriate)

	Specialist responsibilities
1	Initiate treatment and prescribing for the first 3 months of treatment.
2	Discuss the benefits and side effects of treatment with the patient.
3	Ask the GP whether he or she is willing to participate in shared care, and discuss the shared care arrangement with the patient & obtain their consent.
4	Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay.
5	Review the patient's condition and monitor response to treatment regularly where indicated.
6	Give advice to the GP on when to stop /adjust treatment.
7	Report adverse events to the MHRA & GP.
8	Ensure that clear backup arrangements exist for GPs to obtain advice and support.
9	Assess patient, establish diagnosis of probable or possible Alzheimer's or Mixed Alzheimer's and Vascular Dementia (excluding other forms of dementia) following full assessment (include cognitive function, brain imaging if indicated, activities of daily living, behaviour and psychiatric symptoms, carer burden).
10	Check availability of carer if required to supervise medication and ensure compliance.
11	To undertake physical health screen and assessment for the first 3 months of treatment.
12	To provide the patient with information on donepezil including a patient information leaflet (PIL). Information on mental health conditions, treatments and medication can be found at: http://www.choiceandmedication.org/awp/
13	Provide counselling to patient and carer about implications of diagnosis; include written information about signs and symptoms, course, prognosis and treatments, local care and support groups, financial and legal advice.
14	The choice and formulation of the AChEi should be a joint decision between the patient, (discuss with carer where patients lack capacity) and the specialist taking into consideration the risks and benefits of the treatment (including the relative potential of individual AChEi to cause side-effects) including the action to be taken should side effects occur.
15	Assess the patient within 3 months once stabilised on treatment, using appropriate cognitive inventories. If there is evidence of improvement/stabilisation from the assessments, discuss the proposal of shared care with the patient (or their carers as appropriate),obtain consent and document in notes. If patient / their carer, declines shared care, then document this too.
16	Discontinue treatment after 3 months where there is no evidence of benefit or there has been a deterioration of

	the condition. Treatment should be withdrawn gradually and patient monitored for any significant deterioration of functioning or worsening of behavioural symptoms. Consider an alternative cholinesterase inhibitor or memantine (please note: these are still currently Red in Swindon).
17	Ensure that arrangements of appropriate blood tests has been made. Blood tests may be taken at the GP surgery providing appropriate communication with the GP and the GP is in agreement with this. The Specialist is responsible for the interpretation and monitoring of these blood test results for the first 3 months of treatment.
18	Review results of any baseline tests and relay any abnormal findings to the GP with appropriate advice.
19	Review concurrent medication for potential interaction prior to initiation of donepezil, including medication patient receives from the GP and purchases OTC or on-line
20	Communicate promptly with the GP/NMP when treatment is changed.
21	To review patient / provide advice through the memory service advice line as requested via the GP.
22	Inform GP/NMP if any appointments are not attended.
23	Any verbal communication between primary care and the specialist team should be confirmed in writing

General Practitioner responsibilities	
1	Reply to the request for shared care as soon as practicable.
2	Prescribe medicine at the dose recommended after the first 3 months
3	Ensure compatibility with other concomitant medication.
4	Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
5	Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
6	Stop treatment / Adjust dose treatment on the advice of the specialist.
7	Report adverse events to the specialist and MHRA.
8	It is recommended good practice for there to be a basic dementia pre-referral assessment screen as per NICE CG 42 i.e. full blood count, electrolytes, Ca2+, glucose, renal function, liver function, thyroid function, vitamin B12, folate, glucose and scans as appropriate, prior to referral to AWP specialist memory service.
9	To provide medical history to include BP; pulse and cardiac assessment, with ECG if clinically indicated, to exclude cardiac problems. Review of vision and hearing to exclude sensory problems, in particular ear wax and cataracts. See monitoring requirements.
10	Check availability of carer to monitor compliance.
11	If the GP decides not to prescribe donepezil, it should still be added to the patients repeat medication as a “non issued’ item for information and safety purposes. For EMIS systems: The quantity should be set to *0 or 1. On the dose line it should read: ‘Hospital prescribing only. Do not prescribe’. For TPP SystemOne, it is entered using the red question mark icon on the medication screen. Once entered, this appears at the bottom of the repeat template screen in a separate in a separate section (and a different colour), however it does not appear on the repeat prescription screen which may be used by prescription clerks. For Vision Enter as a 1:1 repeat, put quantity as 1 tablet, on the dose line it should read: ‘Hospital prescribing only. Do not prescribe’. This process should also be done during the stabilisation period before the GP takes over the prescribing.
12	Monitor response to treatment including changes in symptoms and behaviour.
13	To request specialist review or seek specialist advice when necessary.
14	Once the patient has been discharged from specialist Mental Health services, advice may be sought from the Primary Care Liaison Service on any aspect of the patient’s mental health that is of concern to the GP/NMP.
15	Monitor patients overall health and compliance with medication.
16	Ask patient / carer about particular problems e.g. side effects, concerns about treatment.
17	Any verbal communication between primary care and the specialist team should be confirmed in writing.

Patient's role	
1	Attend all appointments with GP and specialist.
2	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3	Share any concerns in relation to treatment with medicine.
4	Inform specialist or GP of any other medication being taken, including over-the-counter products or those purchased on-line.
5	Report any adverse effects to the specialist or GP whilst taking the medicine.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:	See below			
Other: **Swindon Primacy Care Liaison service**	01793 835787			
Swindon Memory Service	01793 327800 (reception and ask to be put through)			
Medication advice – a separate system for advice is in the process of being set up, in the meantime contact the Victoria centre 01793 327800 and ask to talk to your surgeries aligned old age consultant.				

SUPPORTING INFORMATION

Summary of condition This Document only appertains to Alzheimer's and Mixed Alzheimer's/Vascular Dementia.It does not relate to dementia in Parkinson's Disease/Lewy Body Dementia.

A note about assessment of Alzheimer's Disease:
When using assessment scales to determine severity of Alzheimer's Disease, 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. This includes the use of alternative assessments that do not rely solely on a cognitive score, such as OT assessments, BADLS, AMPS and LACLs.

Licensed indications - Please also refer to the current BNF and Summary of Products Characteristics (SPC) for full prescribing information on donepezil: www.medicines.org.uk.

Donepezil, is licensed for the symptomatic treatment of mild to moderately severe Alzheimer's disease.
Neither cholinesterase inhibitors nor memantine should be used for the treatment of pure vascular dementia, or frontotemporal dementia except as part of clinical trials.

Expected / established place in local treatment pathway - Donepezil is the only treatment where a shared care arrangement is being sought. This is because of the cost and simplicity of dosing. The other cognitive ehnancers- Galantamine, Rivastigmine and memantine will remain prescribed by secondary care

Dosage and administration
Donepezil is licensed for once daily oral administration.
Usual dosage schedule is initially 5mg once a day at bedtime, increased if necessary after one month to a maximum of 10mg daily.

Contra-indications and precautions for use

Donepezil hydrochloride is contraindicated in patients with a known hypersensitivity to donepezil hydrochloride, piperidine derivatives, or to any excipients used in the formulation.

Donepezil should not be used in pregnancy unless clearly necessary. Women on donepezil should not breast feed

Cardiovascular disease:
May cause bradycardia, Special care in sick sinus syndrome and supraventricular conduction disorders.
Gastrointestinal disorders:
May enhance pre-disposition to peptic ulceration. Patients at risk should be monitored for symptoms.
Pulmonary disorders:
May cause broncho constriction. Caution in asthma and COPD.
Movement disorders:
May exacerbate extrapyramidal symptoms including worsening of parkinsons disease.
Urological:
Bladder outflow obstruction or recovering from bladder surgery.Avoid in urinary retention or history of prostatic condition.
Renal impairment:
No dose adjustment needed.
Hepatic impairment:

Due to possible increased exposure in mild to moderate hepatic impairment dose escalation should be performed according to individual tolerability. There are no data for patients with severe hepatic impairment.

Neurological conditions

There is potential to cause generalised convulsions (seizure activity may also be a manifestation of Alzheimer's disease)

Side-effects

Please note that the following convention has been used for the classification of side-effects: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥ 1/10,000 to <1/1000) and very rare (<1/10,000).

The most common adverse effects include diarrhoea, nausea, vomiting, muscle cramps, dyspepsia, syncope, fatigue, rash, pruritis, urinary incontinence, insomnia, anorexia, weight loss, dizziness and headache. Hallucinations, agitation, aggressive behaviour, abnormal dreams and nightmares have also been reported and have been resolved on reduction or discontinuation of treatment.

Weight loss is also associated with Alzheimer's disease itself and therefore patients' weight should be monitored during therapy (if clinically appropriate).

Refer patient back to the specialist if any of these side-effects cause concern. Refer to the SPC for a full list of adverse effects & further information http://www.medicines.org.uk.

This medicine does not have black triangle (▼) status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Monitoring

Parameter / test	By Primary Care	By Specialist	By Primary care
	Baseline	**Within 3 months after initiation of treatment then periodically**	**Annual as clinically relevant**
Blood pressure	✓	Assess on-going efficacy through periodic assessments as clinically indicated.	✓
Pulse	✓		✓
ECG	✓		✓
Vision and hearing assessment	✓		✓
Calcium	✓		✓
ESR	✓		✓
Folate	✓		✓
Full Blood Count	✓		✓
Glucose	✓		✓
Renal function / U&Es	✓		✓
Liver function	✓		✓
Personal / Family history	✓		✓
Thyroid function	✓		✓
Urinalysis for infection and glucose	✓		✓
Vitamin B_{12}	✓		✓
Weight	✓		✓

Drug Interactions

1. Plasma concentrations of donepezil are increased by potent inhibitors of CYP2D6 (e.g. quinidine, fluoxetine) and CYP3A4 (e.g. ketoconazole, itraconazole and erythromycin).
2. Patients may experience an increased incidence of cholinergic side-effects, mainly nausea and vomiting and a reduction in the dose of the acetylcholinesterase inhibitor may be considered.
3. Acetylcholinesterase inhibitors should **not** be administered with anticholinergic medication due to the antagonism of effect (e.g. hyoscine, dicycloverine, orphenadrine, procyclidine, propantheline). When the patient is taking a drug with anticholinergic properties (e.g. antipsychotics, tricyclics) the relative benefits of taking acetylcholinesterase inhibitors alongside these should be assessed.
4. Enzyme inducers, such as rifampicin, phenytoin, carbamazepine and alcohol may reduce the levels of donepezil.

5. Concomitant use of drugs with anticholinergic properties (e.g. tricyclics, antipsychotics) should be assessed as side effects are exacerbated.
6. Increased propensity for gastrointestinal bleeds with NSAIDs.
7. There is also the potential for synergistic activity with concomitant treatment involving medications such as succinylcholine, other neuro-muscular blocking agents or cholinergic agonists or beta blocking agents which have effects on cardiac conduction.

Cost

Please see current drug tariff for current FP10 prices http://www.ppa.org.uk/ppa/edt_intro.htm

Drug Tariff (October 2014) for 28 days' supply

Drug name, strength and formulation	Cost (£)
Donepezil 10mg oro-dispersible tablets	9.77
Donepezil 10mg tablets	1.76
Donepezil 5mg oro-dispersible tablets	7.32
Donepezil 5mg tablets	1.33

Advice to patient

The oro-dispersible formulation of donepezil should be placed on the tongue, allowed to disperse and swallowed.

References

1. NICE TA 217 Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review) http://www.nice.org.uk/Guidance/TA217
2. NICE CG 42 Dementia Supporting people with dementia and their carers in health and social care. http://www.nice.org.uk/guidance/CG42
3. Dr P Jeyapaul Consultant Psychiatrist Liaison and Later Life SBU, Shared care guideline: For the management of patients receiving cholinesterase inhibitors (donepezil tablets, rivastigmine (twice daily capsules and once daily patch) and galantamine (twice daily tablets and once daily XL capsules) and memantine tablets.
4. Joy Crane Interface pharmacist, BCAP Shared Care Guidelines for cholinesterase inhibitors for Alzheimer's Disease September 2012. http://www.awp.nhs.uk/advice-support/medicines/shared-care/
5. Summary of Products Characteristics (SPC) www.medicines.org.uk
6. Drug tariff http://www.ppa.org.uk/ppa/edt_intro.htm

Author

Original document prepared by Bethan Shepherd, Formulary Pharmacist, AWP
Mental Health NHS Trust May 2012 with working group. Modified by Dr S. Manchip (consultant psychiatrist), Terri Turner (specialist pharmacist) for the Swindon area, & Bethan Shepherd, Formulary Pharmacist – August 2014

Date written

Final draft 26.09.14 at AWP 'Medicines Optimisation Group' meeting. Final version V1.0 approved 16.10.14 at 3Ts

Date of review

Two years from date of approval (October 2016) by 3Ts or earlier if guidance changes.