Powys Shared Care Protocol

Acetylcholinesterase (AChE) Inhibitors – DONEPEZIL, GALANTAMINE & RIVASTIGMINE

for the treatment of mild to moderate Alzheimer's Disease

	✶PLEASE CHECK http://howis.wales.nhs.uk/sitesplus/867/page/42689 FOR THE LATEST VERSION OF THIS PROTOCOL✶
General guidance	The *Powys Primary Care Drugs and Therapeutics Committee* have endorsed this protocol. It outlines the shared care arrangements for patients initiated on **acetylcholinesterase (AChE) inhibitors**: 1. **Donepezil (Aricept®)** Summary of Product Characteristics (SmPC) available at: http://www.medicines.org.uk/EMC/medicine/577/SPC/Aricept+Tablets/ 2. **Galantamine (Reminyl® and Reminyl XL®)** SmPC available at: http://www.medicines.org.uk/EMC/medicine/10335/SPC/Reminyl+Tablets/ 3. **Rivastigmine capsules (Exelon®)** SmPC available at: http://www.medicines.org.uk/EMC/medicine/1284/SPC/Exelon/ **Rivastigmine transdermal patches (Exelon®)** http://www.medicines.org.uk/EMC/medicine/20232/SPC/Exelon+4.6+mg+24h+and+9.5+mg+24h+transdermal+patch/ It should be read in conjunction with the: 1. *Shared Care Agreement Form* – AChE inhibitors. 2. SmPC (Data Sheet) for the corresponding drug. 3. NICE Technology Appraisal Guidance 217 (March 2011): http://guidance.nice.org.uk/TA217 4. NICE Dementia Guidelines: http://www.nice.org.uk/CG42
1. Licensed indication	Donepezil (Aricept®), galantamine (Reminyl® and Reminyl XL®) and rivastigmine capsules (Exelon®) are all licensed for the symptomatic treatment of mild to moderately severe Alzheimer's dementia. **Rivastigmine** capsules (not the transdermal patches) are also licensed for the symptomatic treatment of mild to moderately severe dementia in patients with idiopathic **Parkinson's disease**
2. Therapeutic use & Background information	AChE inhibitors delay the breakdown of acetylcholine in the synaptic cleft and improve neurotransmission in patients suffering from mild to moderate Alzheimer's disease. This may improve cognitive function and stabilise activities of daily living and a global rating scale. AChE inhibitors do not delay disease progression. Their use in the adjunctive treatment of mild to moderate Alzheimer's disease has been recommended by NICE in TAG217. AChE inhibitors are used as part of an overall care plan that addresses the psychological and social as well as medical and other needs of patients with Alzheimer's disease. • Patients will be assessed by a specialist, usually through the older adult mental health team.
3. Contra-indications and Cautions	Patients with a **known hypersensitivity** to donepezil hydrochloride (or other piperidine derivatives), galantamine, rivastigmine (or other carbamate derivatives) or to any excipients used in the formulations. Severe hepatic (Child-Pugh score > 9) and severe renal (creatinine clearance < 9ml/min) should also be considered contraindications.
4. Typical dosage regimen (adults)	Initiation and dose adjustment will be the responsibility of Secondary care. **All dose adjustments will be done by secondary care unless directions have been specified in the medical letter to the GP.**

Donepezil (tablets)
Initially 5mg once daily, increased if necessary after one month to 10mg daily

Galantamine Standard Release (tablets or oral solution)
Initially 4mg bd for 4 weeks, increased to 8mg twice daily for 4 weeks.
Maintenance 8 – 12mg twice daily (according to response and side effects).
Galantamine Modified Release (capsules)
Initially 8mg od for 4 weeks increasing to 16mg od for 4 weeks.
Maintenance 16 – 24mg od (according to response and side effects).

Rivastigmine (capsules or oral solution)
Initially 1.5mg bd increased in steps of 1.5mg bd at intervals of at least 2 weeks according to response and side effects.
Usual range 3 – 6mg bd. Max 6mg bd.
Rivastigmine (transdermal patch)
Initially 4.6mg/24 hours increasing to 9.5mg/24 hours if necessary and tolerated after 4 weeks.
Rivastigmine - if dosing is interrupted for more than a few days, reintroduce with initial dose and increase gradually.

Duration of treatment: Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.

5. Drug interactions
For a comprehensive list consult the BNF or SPC

Muscle relaxants
Antimuscarinic drugs
Beta-blockers
Plasma concentration of galantamine and donepezil is possibly increased by erythromycin, paroxetine, fluoxetine, itraconazole and ketoconazole (and other CYP2D6, CYP3A4 inhibitors).
Plasma concentration of galantamine and donepezil is possibly reduced by rifampicin, phenytoin, phenobarbitone and carbamazepine (and other CYP2D6, CYP3A4 inducers).

6. Adverse drug reactions

Most serious toxicity is seen with long-term use and may therefore present first to GPs. In the event if an adverse reaction occurring, please contact the Specialist department.

AChE inhibitors can cause unwanted dose-related cholinergic effects and should be started at a low dose and the dose increased according to response and tolerability.

SIDE-EFFECTS and ADVERSE REACTIONS for oral AChEIs: DONEPEZIL, GALANTAMINE & RIVASTIGMINE *Clinical condition (reported frequency)*	***Management***
Common (10-15%) – nausea, vomiting, anorexia, diarrhoea, abdominal pain, dyspepsia, weight loss; fatigue, drowsiness, insomnia, sleep disturbance; headache, dizziness, malaise; rhinitis; muscle cramps, asthenia; urinary incontinence; ***Rarely –*** agitation, confusion, depression; tremor, extrapyramidal symptoms and exacerbation of Parkinson's Disease, paraesthesia, tinnitus, leg cramps ***Very rarely*** – sweating	**Reduce dose initially, stop drug if persistent.**
Common – syncope, fever ***Less commonly –*** palpitation, cerebrovascular disease, gastric and duodenal ulcers, ***Rarely –*** aggression, hallucinations; bradycardia; hepatitis; potential for bladder outflow obstruction; rash, pruritus ***Very rarely –*** hypotension, hypertension; dysphagia,	**Stop drug and discuss**
Less commonly – angina pectoris, arrhythmias, sino-atrial block, AV block, myocardial infarction ***Rarely –*** seizures, hypokalaemia, ***Very rarely –*** gastro-intestinal bleeding, pancreatitis	**Stop drug and seek urgent attention**

NOTE: RIVASTIGMINE TRANSDERMAL PATCH	***Management***

	Clinical condition | | ***Side-effect profile as above.*** ***Less likely to cause gastro-intestinal disturbance, but rash and local skin reactions may be more common*** | **Reduce dose (i.e. patch size) initially. Stop drug if persistent & discuss** All serious adverse events should be reported to the MHRA/CHM using the 'Yellow Card' scheme.
7. Baseline investigations	**To be undertaken by GP, <u>prior to referral</u> for memory or psychiatric assessment:** 1. Physical examination 2. FBC, U&Es, creatinine, eGFR measurement, LFTs, TFTs, B12/Folate, calcium and phosphate 3. ECG if history of cardiac disease and arrhythmia 4. Chest X-ray if history of severe lung disease. Only if none available in last 12 months. Baseline brief cognitive examination – carers' views on the patient's condition at baseline should be sought. The Quality and Outcomes Framework for the nGMS contract 2011-12 includes indicator DEM3 for the ongoing monitoring of dementia patients: **DEM3**: The percentage of patients with a new diagnosis of dementia (from 1 April 2011) with a record of FBC, calcium, glucose, renal and liver function, thyroid function tests, serum vitamin B12 and folate levels **recorded 6 months before or after** entering on to the register. The purpose here is to exclude a potentially reversible or modifying cause for the dementia and to help exclude other diagnoses (e.g. delirium). Reversible or modifying causes include metabolic and endocrine abnormalities (e.g. vitamin B12 and folate deficiency, hypothyroidism, diabetes and disorders of calcium metabolism).
8. Ongoing Monitoring	**<u>Specialist:</u>** Once on stable dose specialist review every 6 months. All patients prescribed AChE inhibitors will remain under Secondary care for monitoring of cognition and mental health. All patients are subject to CPA review, which includes review of carer needs. Decisions to discontinue treatment due to lack of effectiveness or deterioration of dementia should be undertaken by Secondary care. **<u>Primary care:</u>** Ongoing and regular review of physical health and well being. Clinical monitoring for adverse effects. Report back to specialist team if required. The Quality and Outcomes Framework for the nGMS contract 2011-12 includes indicator DEM2 for the ongoing monitoring of dementia patients: **DEM2**. The percentage of patients diagnosed with dementia whose care has been reviewed in the preceding 15 months. The review should address four key issues: i. An appropriate physical and mental health review for the patient. ii. If applicable, the carer's needs for information commensurate with the stage of the illness and his or her and the patient's health and social care needs. iii. If applicable, the impact of caring on the care-giver. iv. Communication and co-ordination arrangements with secondary care (if applicable)
9. Pharmaceutical aspects	Do not store medication above 30°C. Do not refrigerate or freeze rivastigmine oral solution.
10. Secondary care contact information	**If stopping the medication or needing advice contact:** Dr Marianne James (BCHB) tel: 01686 617240 Dr Mahmoud Ahmed (ABHB) tel: 01874 712472 Dr Cathryn Jani (ABHB) tel: 01874 712472

	Dr Chineze Ivenso (ABM UHB) tel : 01267 237481
11. Criteria for shared care	**Only specialists in the care of dementia should initiate treatment.** Prescribing responsibility will only be transferred from Secondary care when: ➢ Treatment has been initiated and established. ➢ Treatment is for a specified indication and duration. ➢ The patient's initial reaction to and progress on the drug is satisfactory. ➢ The GP has agreed in writing in each individual case that shared care is appropriate. ➢ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.
12. Responsibilities of initiating consultant	1. To undertake memory and psychiatric assessment and confirm a likely diagnosis of Alzheimer's disease. 2. To advise the patient and carer on potential side effects and the action to be taken should they occur. 3. To identify a suitable person or process to ensure adherence/compliance with treatment where the patient cannot manage on their own. 4. To ensure the patient and carer understands that treatment will be monitored and may be stopped if no objective evidence of improvement occurs. 5. To confirm the patient's understanding and consent to treatment or to discuss with carer(s) where patient lacks capacity. 6. To initiate the AChE inhibitor and make any dosage adjustments. Treatment should normally be started with the AChE inhibitor with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started). An alternative AChE inhibitor could be prescribed if it is considered appropriate when taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles. 7. Once the patient has reached a stable dose of the AChE inhibitor, to send the Shared Care Agreement Form (*copy below*) to the GP. 8. Provide GP with: • Diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. • Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment • Advice on when to stop the medication. 9. At point of transfer of prescribing to the GP, ensure the patient has a minimum of 4 weeks supply of medication. 10. Ongoing monitoring in respect of continued efficacy of the AChE inhibitor**.** Initial review at **3 months or sooner** to make continuation decision. Once on stable dose thereafter regular specialist review **every 6 months** (maximum 12 months gap) in accordance with NICE guidance (i.e. using cognitive, global, functional and behavioural assessment and seeking carers' views on the patient's condition). 11. To communicate any information on changes to the GP. 12. To provide advice to the GP at any stage when needed. 13. To discontinue AChE inhibitor if it is unsuitable for the patient for reasons of efficacy (based on an appropriate method of assessment) or tolerability. Medication should be withdrawn gradually on discontinuation.
13. Responsibilities of Primary Care	1. To undertake baseline physical health monitoring (as outlined in Section 7) and brief cognitive examination prior to referral. Ensure test results are sent with referral. 2. To refer any patient on an AChE inhibitor transferred to the area to the specialist team. 3. To respond to the shared prescribing request within 7 days if unable to accept shared care. 4. Once the patient is on stable dose, to prescribe and monitor the chosen AChE inhibitor in accordance with this protocol, subject to ongoing specialist review (as above). Patient monitoring is an option in The Quality and Outcomes Framework for the nGMS contract 2011-12 (*see section 8 above*).

	5. To be vigilant for potential drug interactions and adverse drug reactions. 6. To notify the responsible clinician of any problems or concerns, or any circumstances that question the need for continued treatment. a. Sudden deterioration in cognitive function. b. Patient intolerance or adverse effects to medication. c. Non-compliance. d. Signs or symptoms of toxicity 7. To discontinue treatment based on advice from the specialist service. 8. To undertake ongoing physical health monitoring and management.
14. Responsibilities of patients/carer	1. To attend hospital and GP clinic appointments. 2. Failure to attend will result in medication being reviewed and possibly stopped on specialist advice. 3. To report adverse effects to their specialist or GP
15. Responsibilities of all prescribers	**Any suspected serious adverse reaction to an established drug should be reported to MHRA via the "yellow card scheme." http://yellowcard.mhra.gov.uk/**
16. Responsibilities of pharmacists	Whenever practicable, to reaffirm with the patient/carer the importance of reporting any unexplained side-effects
17. Supporting documentation / information	**Individual Patient Information Leaflets on the CEIs:** **Donepezil (Aricept®):** http://www.medicines.org.uk/EMC/medicine/2576/PIL/Aricept+Tablets/ **Galantamine:** http://www.medicines.org.uk/EMC/medicine/10338/PIL/Reminyl+Tablets/ **Rivastigmine capsules:** http://www.medicines.org.uk/EMC/medicine/8094/PIL/EXELON+1.5mg%2c+3mg%2c+4.5mg%2c+6+mg+Hard+Capsules/ **Rivastigmine patches:** http://www.medicines.org.uk/EMC/medicine/20403/PIL/Exelon+4.6+mg+24h+and+9.5+mg+24h+transdermal+patch/ **Other information:** NICE technology appraisal guidance 217 (March 2011): Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease: http://guidance.nice.org.uk/TA217 NICE Clinical Guideline 42 (November 2006 amended to incorporate the updated TA217) Dementia: Supporting people with dementia and their carers in health and social care: **http://www.nice.org.uk/CG42**
18. GP request letter	**Shared Care Agreement Form – Attached below**

Shared Care Agreement Form

CONSULTANT REQUEST

To: Dr.

Your patient:	**NHS No. (10digit):**
was seen on:	
with a diagnosis of:	
I recommend that the following acetylcholinesterase inhibitor drug is initiated:	

This drug has been accepted as suitable for shared care by the *Powys PCD&T Committee* I agree to the responsibilities set out in the Powys Shared care Protocol (*copy attached*). This should be read in conjunction with the definition of shared care at: **http://www.wales.nhs.uk/sites3/Documents/371/Doc%202%20Defining%20shared%20care.pdf**

I am requesting your agreement to sharing the care of this patient. The preliminary tests set out in the protocol have been carried out. I am currently prescribing the stabilising treatment.

I would like you to undertake treatment from:
The initial treatment will be:
The baseline tests are:

If you undertake treatment I will reassess the patient in ____ weeks. You will be sent a written summary within 14 days. I will accept referral for reassessment at your request.

The medical staff of the department are available at all times to give you advice.

Consultant Name:	**Signature and date:**
Department:	
Contact Telephone Nos:	

GP RESPONSE (*Please circle the appropriate number below detailing your response*)

1. I am willing to undertake shared care for this patient, as set out in the Shared Care Protocol.
2. I would like further information. Please contact me on: _____
3. I am unable to undertake shared care for this patient because: (*Please state*)

_____

G.P. Signature _____ Date _____

Practice Address/Stamp _____

PLEASE RETURN WHOLE COMPLETED FORM OR A COPY TO THE REQUESTING CONSULTANT WITHIN 2 WEEKS