Shared Care Protocol for the Prescription of Memantine for Alzheimer's disease

1. REFERRAL CRITERIA

Patients of any age that are suspected to be suffering from moderate to severe Alzheimer's disease will be referred to Older People's Mental Health Service for assessment.

2. PATIENT ELIGIBILITY

- Those patients with moderate Alzheimer's disease **intolerant** of acetylcholinesterase inhibitors (AChEI) or in whom their use is **contraindicated**.
- Patients with **severe** Alzheimer's disease

3. AREAS OF RESPONSIBILITY

Primary Care responsibilities	Secondary care responsibilities
Identifying patients who are suspected to be suffering from moderate to severe Alzheimer's disease. Referral to specialist mental health services for diagnosis and assessment. Prescribing of Memantine following initiation and stabilisation by secondary care with documented evidence of clinical effectiveness. **LFTs** Approximately 1 in a 100 patients taking Memantine incur raised liver function tests. This is usually clinically insignificant and **does not** require screening / monitoring. If raised liver function tests are coincidentally detected, the GP should **stop** Memantine and refer back to secondary care for review.	Diagnosis of moderate to severe Alzheimer's disease. Assessment of mental state. Initiation of treatment with Memantine. Dose adjustment to maintenance dose. Assessment of effectiveness* of treatment at minimum of one month after reaching maintenance dose. Reassessment of effectiveness* of treatment on a regular basis to ensure continuing benefit. **Appropriate scales such as the Montreal Cognitive Assessment (MoCA), Severe Impairment Battery (SIB), The Neuropsychiatric Inventory (NPI), and The Bristol Activities of Daily Living (BADL) Scale should be used to help judge effectiveness.* Discontinuation of treatment if ineffective or no longer indicated. Consideration of clinical significance of raised liver function tests.

4. COMMUNICATION AND SUPPORT

Working hours hospital contact: Chrissy Taylor, Memory Services Manager, Howarth House, Brinsworth Lane, Rotherham, S60 5BX **Tel number:** 01709 302955 **Fax:** 01709 830213 **Email:** chrissy.taylor@rdash.nhs.uk
Out of hours contacts and procedures: On call psychiatric staff via the access team **Tel number:** 01709 302670

5. CLINICAL INFORMATION

Prescribed indications	Treatment of patients with moderate to severe Alzheimer's disease.
Exclusions (not covered by SCP)	"Dual prescribing" of Memantine with AChEI.
Therapeutic summary	Memantine is an NMDA receptor antagonist in the presence of abnormal glutamate concentrations at the synapse: the effect of which is to normalise neuronal action potentials and function
Contraindications	Hypersensitivity to active substance or any of the excipients.
Special warnings and precautions	Not recommended for patients with severe renal impairment. Caution is recommended with patients suffering from epilepsy, or a history of convulsions. Clinical data is limited on patients with myocardial infarction, congestive heart failure and uncontrolled hypertension **Patients with these conditions should be closely supervised.**
Overdose	Symptomatic treatment.
Elimination	Mainly unchanged via the kidneys.
Dose & Route of administration	Treatment starts with 5 mg daily for 1st week; the 2nd week 10 mg daily; the 3rd week 15 mg daily and from the 4th week 20mg daily. Maintenance dose is 20 mg od taken with or without food. Reduce dose to 10mg daily in patients with an eGFR < 30mls/min.
Presentation	Treatment initiation ("starter") pack 7 x 5mg, 7 x 10mg, 7 x 15mg, 7 x 20mg orally as tablets

Duration of treatment	Treatment should only be continued when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.
Side effects	The most frequently occurring adverse events with a higher incidence in the memantine group than in the placebo group were dizziness (6.3% vs 5.6%, respectively), headache (5.2% vs 3.9%), constipation (4.6% vs 2.6%), somnolence (3.4% vs 2.2%) and hypertension (4.1% vs 2.8%). Other adverse drug reactions include • Common (between 1/10 and 1/100) balance disorders, dyspnoea, elevated LFTs, • Uncommon (between 1/100 and 1/1,000) fungal infections, confusion, hallucinations, abnormal gait, cardiac failure, venous thrombosis/thromboembolism, vomiting, fatigue, anxiety, increased muscle tone, cystitis and increased libido • Very rare (less than 1/10,000) or unknown seizures, pancreatitis, psychosis, depression, suicidal ideation also reported.
Monitoring Requirements	Regular review of cognitive, global, functional & behavioural symptoms.
Clinically relevant drug interactions	Concomitant use of amantadine, ketamine or dextromethorphan should be avoided. Effects of L-dopa, dopaminergic agonists and anticholinergics may be enhanced. Effects of barbiturates and neuroleptics may be reduced. Effect of dantrolene and baclofen may be modified. Plasma levels of cimetidine, ranitidine, procainamide, quinidine quinine and nicotine may be increased. Urinary pH increase may elevate plasma levels of Memantine.
Supply, storage and reconstitution instructions	No special supply, storage or reconstitution instructions
Prepared by (December 2013)	Jerry Seymour, Consultant Psychiatrist, RDaSH Andrew Houston, Senior Pharmacist, RDaSH
Updated by (July 2015)	John Bottomley – Consultant Psychiatrist, Clinical Director, RDaSH Raz Saleem – Prescribing Advisor, NHS RCCG
Review	This document will be reviewed in light of any new evidence / guidelines OR by July 2020
References	NICE Guideline 42 Dementia (CG 42): Supporting people with dementia and their carers in health and social care. November 2006 (revised March 2011). NICE Technology Appraisal 217 (TA 217): Alzheimer's disease - donepezil, galantamine, rivastigmine and memantine. March 2011.

Memantine Initiation, Continuation and Discontinuation protocol

This document is to be used in conjunction with:

- NICE TAG 217 on the use of Memantine in Alzheimer's Disease Dementia
- RDASH Medicines Management Committee approved ICP "Memantine Initiation and Monitoring" agreed 06/05/11
- RDASH ACHEI Shared Care Protocol March 2011 (page 1-3)
- RDASH BPSD Guidance

Initiation criteria

The patient meets the criteria in the ICP "Memantine initiation and monitoring" in moderate to severe Alzheimer's disease

ACHEI therapy is contraindicated by reason of medical co-morbidity in moderate disease
Proven intolerance to ACHEI therapy in moderate disease
Behaviour that challenges and other non-pharmacological / pharmacological therapies are inappropriate, ineffective or contra–indicated in moderate to severe disease
Evidence of psychosis and other non-pharmacological / pharmacological therapies are inappropriate, ineffective or contra–indicated in moderate to severe disease
Severe Alzheimer's disease (MOCA <10/30 or equivalent assessment of severity)

Below are baseline assessments to complete before initiation with indicated scores of moderate to severe disease. At least one must indicate moderate to severe disease and that scale must be used at follow up to assess treatment response.

1) Montreal Cognitive Assessment (MOCA) or equivalent test of cognitive function indicating moderate disease, MOCA 10-20/30,
2) MOCA or equivalent test indicating severe disease, MOCA <10/30, severe impairment battery (SIB) <70/100
3) Neuropsychiatric inventory (NPI) with a score of 4 or above on any of the Delusions, Agitation or aggression , or Irritability / lability sub-scales
4) Bristol Activities of Daily Living score (BADL) >20/60
5) An overall clinical global impression should be stated of the disease stage

Patients should be reviewed at 3 months of initiation and then every 6 months using the criteria below.

Continuation criteria

The patient meets the criteria in the ICP "Memantine initiation and monitoring" in moderate to severe Alzheimer's disease by response in at least one domain which is clinically relevant. Improvement / stabilisation of cognitive function better than expected natural decline e.g. less than expected decline in MOCA score of >5 points in 12 months in moderate disease or 5 points on the SIB over 6 months in severe disease.

Meaningful improvement/ stabilisation of functional ability as evidenced by improvement, stabilisation 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 stabilisation in severe disease.

Reduction in aggressive behaviour that challenges and/or psychosis as evidenced by NPI improved scores of 2 or more in the relevant subscale over 6 months.

An overall clinical global impression of stabilisation or improvement must be stated.

Discontinuation criteria

Discontinuation must be discussed first with the carers, family, and with the patient wherever possible.

1) Adverse reaction to the medication
2) Lack of compliance with the medication lack of evidence of efficacy i.e. the patient does not fulfil the criteria for continuation stated above
3) Patient is on an end of life care pathway.
4) If the treatment is for cognitive problems predominantly a MOCA of <5/30 or SIB score of <30/100. GPs may wish to use any recognised cognitive tests (eg 6 item CIT) to determine cognitive decline and likely continued benefit of Memantine.
5) 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

Any help or discussion about a particular patient, please contact the patient's sector team on 01709 302902 or the nursing home liaison team on 01709 447300

Information for General Practice

Integrated Care Pathway - Memantine initiation and monitoring

- This document outlines the pathway which RDaSH follow when initiating and monitoring the management of dementia by prescribing memantine according to the shared care protocol. Prescribing should be in accordance with NICE Technology Appraisal TA217 (Alzheimer's disease - donepezil, galantamine, rivastigmine and memantine) NICE guidance TA217

Assessment & Screening Stage

M1

INCLUSION CRITERIA:

1. Full History documented
2. Disease stage appropriate - cognitive, BPSD & ADL's assessment including Mental State Examination
3. Relevant physical examination in primary or secondary care
4. Locally agreed dementia care pathway investigations including blood tests
5. Medication review

M2

SERVICE USER MEETS ALL 4 CRITERIA:

1. Moderate to severe Alzheimer's Disease (ICD 10: F00.0 or F00.1/F00.2/F00.9)(As judged by MOCA score of <20 or global assessment of functional ability)
2. **No** uncontrolled epilepsy
3. **No** severe renal impairment (CKD4/5).If eGFR<30mls/min maximum dose is 10mg od

AND MEETS AT LEAST ONE OF THE FOLLOWING CRITERIA:

M3

- ACHEI therapy is contraindicated by reason of medical co-morbidity in moderate disease
- Proven intolerance to ACHEI therapy in moderate disease
- Behaviour that challenges and other non-pharmacological / pharmacological therapies are inappropriate, ineffective or contra–indicated in moderate to severe disease
- Evidence of psychosis and other non-pharmacological / pharmacological therapies are inappropriate, ineffective or contra–indicated in moderate to severe disease
- Severe Alzheimer's disease (MOCA <10 or equivalent assessment of severity)

Initiation Phase

ASSESSMENT HAS OCCURRED AND THE SERVICE USER MEETS:

All criteria from **M2 and one** criteria from **M3**

- Mental capacity of user assessed in line with Trust policies/protocols.
- Need for a trial of memantine explained to service user (and carer / advocate where appropriate), together with the potential risks and benefits
- Advanced directive considered where available and arrangements made to facilitate the writing of one if appropriate.

Decision to commence memantine collaboratively made with consideration to:

- U+E and eGFR results
- Drug interactions.
- Mental capacity + informed consent
- Advanced plan / directive

And appropriate written information given if appropriate.

- Starting dose…… Target Dose……
- Titration prescribed as per BNF and SPC and follow up appointment made to review titration.
- Date/ interval……

Consider Supplementary prescribing with appropriate clinical management plan

GP informed of treatment plan and provided with written authorisation that the prescribing of Memantine has been approved through RDaSH approval process.