RIVASTIGMINE (oral) for treatment of dementia in patients with Parkinson's disease

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).
This guideline reinforces the basic premise that:
When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the "sharing of information with the individual GP and their mutual agreement to the transfer of care."
These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Indications:	**Dosage and administration:**
Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease.	Initial dose: 1.5mg twice a day with morning and evening meals. Titration: The starting dose is 1.5 mg twice a day. If this dose is well tolerated after a minimum of two weeks of treatment, the dose may be increased to 3 mg twice a day. Subsequent increases to 4.5 mg and then 6 mg twice a day should also be based on good tolerability of the current dose and may be considered after a minimum of two weeks of treatment at that dose level. Maintenance dose: The effective dose is 3 to 6 mg twice a day; to achieve maximum therapeutic benefit patients should be maintained on their highest well tolerated dose. The recommended maximum daily dose is 6 mg twice a day. Maintenance treatment can be continued for as long as a therapeutic benefit for the patient exists. Rivastigmine **oral solution** should be administered twice a day, with morning and evening meals (Oral solution is significantly more expensive that the tablets- restricted by the CCG for patients with swallowing difficulties).

Additional Information:
-Rivastigmine oral solution and rivastigmine capsules may be interchanged at equal doses.
-Re-initiation of therapy: If treatment is interrupted for more than three days, it should be re-initiated at 1.5 mg twice daily. Dose titration should then be carried out as per protocol.
Oral solution must be used within one month of opening.

Monitoring requirements:
The clinical benefit of rivastigmine should be reassessed on a regular basis, especially for patients treated at doses less than 3 mg twice a day. If after 3 months of maintenance dose treatment the patient's rate of decline in dementia symptoms is not altered favourably, the treatment should be discontinued. Discontinuation should also be considered when evidence of a therapeutic effect is no longer present.

Because of the risk of bradycardia, the pulse must be monitored regularly, and discontinued immediately if the pulse falls below 50 beats per minute, or if there is evidence of developing heart block.

The patient's weight should be monitored during therapy with rivastigmine capsules and solution.

Action to be taken if abnormal results/adverse effects:
In overdose accompanied by severe nausea and vomiting, the use of antiemetics should be considered. Symptomatic treatment for other adverse reactions should be given as necessary.
In massive overdose, atropine can be used. An initial dose of 0.03 mg/kg intravenous atropine sulphate is recommended, with subsequent doses based on clinical response. Use of scopolamine as an antidote is not recommended.

Contraindications:
The use of this medicinal product is contraindicated in patients with known hypersensitivity to the active substance rivastigmine, to other carbamate derivatives or to any of the excipients

Significant Drug interactions:
Rivastigmine may exaggerate the effects of succinylcholine-type muscle relaxants during anaesthesia. Caution is recommended when selecting anaesthetic agents. Possible dose adjustments or temporarily stopping treatment can be considered if needed.
Should not be given concomitantly with other cholinomimetic substances and might interfere with the activity of anticholinergic medicinal products
Rivastigmine may inhibit the butyrylcholinesterase mediated metabolism of other substances.
For full list of drug interactions please refer to the SPC.

Cautions:
-No dose adjustment is necessary for patients with mild to moderate renal or hepatic impairment. However, these populations dosing recommendations are to titrate according to individual tolerability and should be closely monitored.
-Care must be taken when using rivastigmine in patients with sick sinus syndrome or conduction defects (sino-atrial block, atrio-ventricular block).
-Rivastigmine may cause bradycardia which constitutes a risk factor in the occurrence of torsade de pointes.
-Rivastigmine may cause increased gastric acid secretions. Care should be exercised in treating patients with active gastric or duodenal ulcers or patients predisposed to these conditions.
-Patients with history of asthma or obstructive pulmonary disease.
-May induce or exacerbate urinary obstruction and seizures.
-The use of rivastigmine in patients with severe dementia associated with Parkinson's disease has not been investigated and therefore use in this patient population is not recommended.

Adverse Effects:
-Dose titration: Adverse reactions (e.g. hypertension and hallucinations in patients with Alzheimer's dementia and worsening of extrapyramidal symptoms, in particular tremor, in patients with dementia associated with Parkinson's disease) have been observed shortly after dose increase. They may respond to omitting one or more doses; if adverse reactions persist, the daily dose should be reduce to the previous well-tolerated dose or treatment may be discontinued.
-Gastrointestinal disorders such as nausea, vomiting and diarrhoea are dose-related, and may occur particularly when initiating treatment and/or increasing the dose, more commonly in women.
-One of the excipients in rivastigmine oral solution is sodium benzoate. Benzoic acid is a mild irritant to the skin, eyes and mucous membrane.
-Monitoring weight loss.
For full list of adverse effects please refer to the SPC.
Any suspected or confirmed adverse drug reactions must be reported via the Yellow Card Scheme at: https://yellowcard.mhra.gov.uk

Specialist responsibilities:
Diagnose condition and discuss with patient the benefits and side effects of treatment with rivastigmine.
On initiation, 28 days of medication to be prescribed (using a hospital outpatient prescription form) at a recommended escalating dose as per clinical discretion, do not increase the dose more than once weekly. Most patients will respond to 6 mg daily though a lower or higher dose may be required for maximum benefit.
Should the patient require oral solution instead of tablets, clearly indicate to the GP the reasoning for this.
Review the patient's condition and initial response to treatment until patient dose is stable.
Once the patient is on a stable dose of rivastigmine a further 28 days' supply of medication should be prescribed (using a hospital outpatient prescription form) and a request sent to the GP to continue treatment at this dose.
Regularly review the patient's condition and monitor response to treatment.

Communicate promptly with GP when treatment is changed.
Advise GPs when to refer back and who to communicate with.
Advise GPs how to stop treatment (see section above and secondary care review section below).
Report adverse events to the CSM.
Ensure that clear backup arrangements exist for GPs for advice and support.

GP's responsibilities:
Reply to the request for shared care as soon as practicable.
Prescribe rivastigmine as recommended.
Monitor patient's response to treatment on maintenance doses only (the team responsible for the titration will be doing the monitoring during initial stages).
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.
Refer back to specialist if condition deteriorates, and monitor if any adverse effects arise.
Aware of side effects and report it to specialist and MHRA.
Stop treatment following a reducing dose course as per specialist advice.

Patient's responsibilities:
Report to the specialist or GP if he or she does not have a clear understanding of the treatment or has concerns in relation to treatment with rivastigmine.
Report any adverse effects to the specialist or GP whilst taking rivastigmine.

Secondary care review: Monthly until patient on a stable dose of treatment and then every six months in movement disorder clinic. Where there is a specific problem, patient may be seen in the community by Parkinson's disease specialist nurse (if appropriate) or return earlier to clinic for review.

Availability:
Rivastigmine 1.5mg capsules, 28 capsule pack costs £1.96 *(Drug Tariff, March 2018)* Rivastigmine 2mg/ml oral solution sugar free, 120ml bottle costs £96.82 *(Drug Tariff, March 2018)* Rivastigmine 3mg capsules, 28 capsule pack costs £2.26 *(Drug Tariff, March 2018)* Rivastigmine 4.5mg capsules, 28 capsule pack costs £23.52 *(Drug Tariff, March 2018)* Rivastigmine 6mg capsules, 28 capsule pack costs £28.78 *(Drug Tariff, March 2018)*

Back up advice and support:	**Telephone**
Parkinson's disease specialist nurse: Dr M O'Neill (Elderly Medicine Consultant and Lead for Elderly Movement Disorders) Dr E Azie (PD Staff Grade)	0151 514 6685 Secretary: 0151 604 7445 Bleep via Arrowe Park Switchboard: 7016

References:
NICE TA Donepezil, galantamine, rivastigmine & memantine for treatment of alzheimers disease, published March 2011, updated May 2016
Rivastigmine SPC https://www.medicines.org.uk/emc/product/8496/smpc (Updated Sept 17 - accessed 04.05.18)
Drug Tariff, March 2018, available at http://www.ppa.org.uk/ppa/edt_intro.htm

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