Rotigotine *(Neupro®)* (TLS Amber)

Shared Care Guidelines: For the treatment of Parkinson's Disease (PD).

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of Rotigotine for Parkinson's Disease is shared between the 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. Patients with PD are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Initiate treatment and provide at least 28 days' supply
2	Discuss the benefits and side effects of rotigotine with the patient.
3	Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient.
4	Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay.
5	Supply monitoring details to the GP
6	Monitor blood pressure at the beginning of treatment
7	Review the patient's condition and monitor response to treatment regularly where indicated.
8	Give advice to the GP on when to stop treatment.
9	Report adverse events to the MHRA.
10	Ensure that clear backup arrangements exist for GPs to obtain advice and support.

	General Practitioner responsibilities
1	Reply to the request for shared care as soon as practicable.
2	Prescribe medicine at the dose recommended.
3	Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease progression) or intolerance to therapy occurs.
4	Liaise with specialist for the following issues: Concerns regarding adverse effects, including skin reactions. Also see point 5 (below) and monitoring requirements.
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 gradually on the advice of the specialist.
7	Report adverse events to the specialist and MHRA.

	Patient's role
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.
4	Heed advice regarding incidence of somnolence or sudden sleep episodes and their impact on lifestyle.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:				
Hospital Pharmacy Dept:	01225 824640			
Other: PD Nurse Specialist	01225 831676			

Points for the GP to pass on to the patient:

Advise patients referred for MRI or cardioversion of need to remove patch for duration of the procedure. See also information regarding somnolence and signs of dopamine dysregulation.

SUPPORTING INFORMATION

Summary of condition and licensed indications.

The medicine is indicated for:

- The treatment of the signs and symptoms of early-stage idiopathic PD as monotherapy (i.e. without Levodopa)
  or
- In combination with Levodopa i.e. over the course of the disease, through to late stages when the effect of Levodopa wears off or becomes inconsistent and fluctuations in the therapeutic effect occur (end of dose or "on-off" fluctuations).
- Rotigotine should be used where transdermal application is considered to be beneficial.

Treatment Aims (Therapeutic plan)

The aim of rotigotine treatment is relief of the signs and symptoms of PD either as monotherapy in early PD or in combination with Levodopa in later stages of PD.
Rotigotine is a novel $D_3/D_2/D_1$ dopamine-receptor agonist delivered through a transdermal patch.
Shared care will increase patient convenience by preventing frequent attendances to hospital for monitoring and to collect prescriptions or drug supplies.
Other benefits of shared care include:

- GP awareness of all medications that their patient is taking
- Patient safety:
  - GP medication records are complete if queries to surgery arise following emergency admission
  - GP medication records complete when checking for drug interactions

Treatment Schedule (including dosage and administration)

Rotigotine patches are available in four strengths: 2mg/24 hours; 4mg/24 hours; 6mg/24hours; 8mg/24 hours. Do not cut the patches.

Rotigotine patches are applied once a day. The patch should be applied at approximately the same time every day. The patch remains on the skin for 24 hours and will then be replaced by a new one at a different site of application.
If the patient forgets to apply the patch at the usual time of the day or if the patch becomes detached, another patch should be applied for the remainder of the day.

For patients requiring rotigotine monotherapy the starting dose is 2mg/24 hours with the dose being increased by 2mg/24 hours at weekly intervals until symptoms are controlled. The optimum daily dose will be determined by the Consultant or Nurse Specialist, but according to the Summary of Product Characteristics (SPC) this is usually at a dose of 6mg/24 hours or 8mg/24 hours.

For patients with more advanced PD requiring combination therapy rotigotine should be initiated at 4mg/24 hours and increased at weekly increments of 2mg/24 hours up to an effective dose up to a maximum of 16mg/24 hours. 4 mg/24 h or 6 mg/24 h may be effective doses in some patients.
For most patients an effective dose is reached within 3 to 7 weeks at doses of 8 mg/24h up to a maximum dose of 16 mg/24 h. For doses higher than 8 mg/24 h multiple patches may be used to achieve the final dose e.g. 10 mg/24 h may be reached by combination of a 6 mg/24 h and a 4 mg/24 h patch.

Treatment with Rotigotine is long term.

When the patient should be referred back to the specialist:

- Concerns regarding adverse effects
- Concerns regarding lack of efficacy
- Significant deterioration in renal or liver function
- Skin reactions

Contra-indications and precautions for use
Contra-indications:
Hypersensitivity to the active substance or to any of the excipients; magnetic resonance imaging or cardioversion (the backing layer of Neupro® patches contains aluminium and skin burns may occur if the patch is not removed).

Precautions:
If a patient is insufficiently controlled while on treatment with rotigotine switching to another dopamine agonist might provide additional benefit.

Dopamine agonists are known to impair the systemic regulation of the blood pressure resulting in postural/orthostatic hypotension. These events were also observed during treatment with rotigotine, however the incidence was similar to that in placebo-treated patients. Syncope was observed in association with rotigotine, but also at a similar rate in patients treated with placebo.
It is recommended to monitor blood pressure, especially at the beginning of treatment, due to the general risk of orthostatic hypotension associated with dopaminergic therapy.

Rotigotine has been associated with somnolence and episodes of sudden sleep onset, particularly in patients with Parkinson's disease. Sudden onset of sleep during daily activities, in some cases without awareness of any warning signs, has been reported. Prescribers should continually reassess patients for drowsiness or sleepiness, as patients may not acknowledge drowsiness or sleepiness until directly questioned. A reduction of dosage or termination of therapy should be carefully considered.

Pathologic gambling, increased libido and hypersexuality have been reported in patients treated with dopamine agonists for Parkinson's disease, including rotigotine.

Hallucinations have been reported and patients should be informed that hallucinations can occur.

Ophthalmologic monitoring is recommended at regular intervals or if vision abnormalities occur.

External heat (excessive sunlight, heating pads and other sources of heat such as sauna, hot bath) should not be applied to the area of the patch.

Application site skin reactions may occur and are usually mild or moderate in intensity. It is recommended that the application site should be rotated on a daily basis (e.g. from the right side to the left side and from the upper body to the lower body). The same site should not be used within 14 days. If application site reactions occur which last for more than a few days or are persistent, if there is an increase in severity, or if the skin reaction spreads outside the application site, an assessment of the risk/benefit balance for the individual patient should be conducted. If there is a skin rash or irritation from the transdermal system, direct sunlight on the area should be avoided until the skin heals. Exposure could lead to changes in the skin color. If a generalised skin reaction (e.g. allergic rash, including erythematous, macular, papular rash or pruritus) associated with the use of Rotigotine is observed, Rotigotine should be discontinued.

Caution is advised when treating patients with severe hepatic impairment, which may result in lower rotigotine clearance. A dose reduction might be needed in case of worsening of the hepatic impairment. Unexpected accumulation of rotigotine levels may also occur at acute worsening of renal function.

Side-effects
At the beginning of therapy dopaminergic adverse reactions such as nausea and vomiting may occur. These are usually mild but if troublesome can be managed by using Domperidone 10mg – 20mg three times a day. This can usually be withdrawn after a few weeks as tolerance develops.

Caution is needed in patients with low blood pressure or pre-existing postural hypotension. Check lying and standing blood pressure measurements if patient reports dizziness or unsteadiness.

Adverse drug reactions (ADRs) reported in more than 10% of patients treated with Rotigotine patch are nausea, dizziness, somnolence and application site reactions.

In trials where the application sites were rotated as reflected in the instructions provided in SPC and package leaflet, 35.7% of 830 patients using the rotigotine, experienced application site reactions. The majority of these reactions were mild or moderate in intensity, limited to the application areas and resulted in discontinuation of treatment with rotigotine in only 4.3% of all subjects receiving rotigotine. See the advice above regarding management of application site reactions and site rotation.
Refer to the SPC for a full list of adverse effects.

Rotigotine was launched in April 2006 and has black triangle (▼) status. All suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Monitoring

Parameter	Frequency of monitoring	Action (adjustment and referral back to hospital)
Lying and standing blood pressure	Pre treatment – by Specialist Once dose stable and if patient reports dizziness of unsteadiness on standing. Check standing BP before adding other antihypertensive medicines.	If symptomatic reduce other antihypertensive medications (if possible) Contact specialist. May need to reduce rotigotine dose (do not discontinue suddenly).
Application site reactions	If problem reported.	Check patient is rotating application site. Contact PD Nurse Specialist.
Sudden onset of sleep or drowsiness	If problem reported and when considering safety for driving.	Seek specialist advice. Advice patient to discontinue driving until medication reviewed by specialist.
Signs of dopamine dysregulation	Consider in context of erratic or unusual compulsive behaviour.	Clarify issues with carer, if appropriate, and contact specialist.
Check for renal or hepatic dysfunction	Routine monitoring not required. Consider if patient unwell.	Contact specialist. May need to reduce rotigotine dose (do not discontinue suddenly).

Drug Interactions

Because rotigotine is a dopamine agonist, it is assumed that dopamine antagonists, such as neuroleptics (e.g. phenothiazines, butyrophenones, thioxanthenes) or metoclopramide, may diminish the effectiveness of Rotigotine, and co-administration should be avoided.

Because of possible additive effects, caution should be advised when patients are taking sedating medicinal products or other central nervous system depressants (e.g. benzodiazepines, antipsychotics, antidepressants) or alcohol in combination with rotigotine.

Rotigotine may potentiate the dopaminergic adverse reaction of L-dopa and may cause and/or exacerbate pre-existing dyskinesia, as described with other dopamine agonists.

Cost

At current prices (excluding VAT), one year's treatment with rotigotine at the following doses is:

2mg/24 hours £927

4mg/24 hours £1,060

6mg/24 hours £1,324

8mg/24 hours £1,713

10mg/24 hours £2,383

12mg/24 hours £2,648

14mg/24 hours £3,038

16mg/24 hours £3,427

References

Summary of Product Characteristics Neupro Transdermal Patch, Schwarz Pharma Limited, January 2007.SPC Neupro patches

Shared Care Guideline for the use of Rotigotine (Neupro) in the Management of Parkinson's Disease. Dorset and Somerset Prescribing Forum

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Document details

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