NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Shared Care Guideline

Rotigotine

Executive Summary

Indication:
- Parkinson's disease, either alone or as an adjunct to co-beneldopa or co-careldopa.

Patient Group:
- Patients with early-stage idiopathic Parkinson's disease (as monotherapy)
- Patients with advanced Parkinson's disease in whom the effects of levodopa have worn off or are inconsistent (as adjunct).
- Patients with Parkinson's disease and dysphagia where it is appropriate to limit oral medication

Dose Adjustments:
- Monotherapy: 2 mg/24 hours increased by 2 mg/24 hours weekly to max. 8 mg/24 hours.
- Adjunct: 4 mg/24 hours increased by 2 mg/24 hours weekly to max. 16 mg/24 hour

GP responsibilities:
- The GP will report any adverse events to the hospital specialist as appropriate.

Hospital responsibilities:
- Monitor for toxicity and efficacy
- Communicate any treatment changes or adverse events to the GP and respond to any request from GP to review the patient due to adverse effects of therapy

Criteria for treatment continuation and definition of treatment failure
The Parkinson's disease specialist team will continue to monitor efficacy, tolerability and appropriateness of rotigotine on a 6 monthly basis, unless more frequent monitoring is required**.**
The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document here

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. Further information about the general responsibilities of the hospital specialist and GP can be found here

1. Scope
Prescribing and monitoring of rotigotine transdermal patches by consultants, specialist nurses and GPs.

2. Aim
To provide advice on the safe prescribing and monitoring of rotigotine for the treatment of Parkinson's disease.

3. Introduction

Rotigotine is a non-ergot derived dopamine receptor agonist, available as a transdermal preparation (patch).

It is licensed for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease as monotherapy (ie without levodopa) or in combination with levodopa, ie over the course of the disease, through to late stages when the effect of levodopa wears off or becomes inconsistent and fluctuations of the therapeutic effect occur (end of dose or 'on-off' fluctuations).

Rotigotine should be initiated and titrated by a consultant neurologist, Parkinson's or neurology specialist nurse or consultant geriatrician, named as being allowed to prescribe (see on-line British National Formulary).

Once a patient has been established on an optimum dose, care will then pass to the primary care team under the continued guidance and support of the Parkinson's disease specialist team.

The only exceptions to this are:

- In the case of patients who have swallowing difficulties or those who have been designated 'nil by mouth', for whom rotigotine patches may be prescribed by **any** doctor, provided that the Trust policy is adhered to and only while an inpatient.
- Under the advice of a Parkinson's specialist for patient in the community who are unable to swallow their usual medicines.

4. Abbreviations

GP General Practitioner
MRI magnetic resonance imaging

5. Dose and Administration

5.1 Administration

- Rotigotine patches are applied once a day at approximately the same time every day. The patch remains on the skin for 24 hours and is then replaced by a new one at a different site of application. The same site should not be used within 14 days. If a 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.
- The patch should be applied to clean, dry, intact healthy skin on the abdomen, thigh, hip, flank, shoulder, or upper arm. Reapplication to the same site within 14 days should be avoided. Rotigotine should not be placed on skin that is red, irritated or damaged.
- The patch should not be cut into pieces

5.2 Adult Dosage

For patients with early stage Parkinson's disease:

- A single daily dose should be initiated at 2mg/24 h and then increased in weekly increments of 2mg/24 h to an effective dose up to a maximal dose of 8mg/24 h.
- 4mg/24 h may be an effective dose in some patients. For most patients an effective dose is reached within three or four weeks at doses of 6mg/24 h or 8mg/24 h, respectively.
- The maximal dose is 8mg/24 h.

For patients with advanced stage Parkinson's disease with fluctuations:

- A single daily dose should be initiated at 4mg/24 h and then increased in weekly increments of 2mg/24 h to an effective dose up to a maximal dose of 16mg/24 h.
- 4mg/24 h or 6mg/24 h may be effective doses in some patients. For most patients an effective dose is reached within three to seven weeks at doses of 8mg/24 h up to a maximum dose of 16mg/24 h.
- For doses higher than 8mg/24 h multiple patches may be used to achieve the final dose e.g. 10mg/24 h may be reached by combination of a 6mg/24 h and a 4mg/24 h patch.

5.3 Withdrawal

Rotigotine should be discontinued gradually. Symptoms suggestive of parkinsonism hyperpyrexia syndrome, whose clinical features are similar to the neuroleptic malignant syndrome, have been reported with abrupt withdrawal of dopaminergic therapy.

The daily dose should be reduced in steps of 2 mg/24 h with a dose reduction preferably every other day, until complete withdrawal.

Further information can be found in the Summary of Product Characteristics
http://www.medicines.org.uk/emc/medicine/27412

6 Adverse Effects

Very Common >1/10	Common >1/100 to <1/10	Uncommon >1/1,000 to <1/100	Rare >1/10,000 to <1/1,000
Dizziness	Asthenic conditions	Hypersensitivity (which may include angioedema, tongue oedema and lip oedema)	Psychotic disorder
Somnolence	Hyperhidrosis	Abdominal pain	Obsessive compulsive disorder
Headache	Erythema	Raised hepatic enzymes (GGT/ALT/AST)	Convulsions
Nausea†	Pruritus	Weight increased	Supra-ventricular tachycardia
Vomiting†	Constipation	Sleep attacks (sudden onset of sleep)	Generalised rash
Application site reactions	Dry mouth	Paranoia	Irritability

Very Common	Common	Uncommon	Rare
	Dypepsia	Sexual desire disorders (hypersexuality/	Delusions
	Hiccough	Increased libido	Delirium
	Orthostatic hypotension	Confusion	Aggressive behaviour/ aggression
	Hypertension	Visual disturbance (blurred vision, visual impairment, Photopsia)	
	Dizziness	Blurred vision	
	Hallucinations	Increased heart rate	
	Anxiety	Atrial fibrillation	
	Insomnia	Hypotension	
	Anorexia	Pruritus	
	Palpitations	Generalised skin irritation	
	Fall	Erectile dysfunction	
	Dyskinesia	Disorientation	
	Syncope		
	Sleep disorders (abnormal dreams/nightmares		
	Peripheral oedema		
	Binge eating and compulsive eating		
	Asthenic conditions (including; malaise, fatigue and asthenia)		

Very Common	Common	Uncommon	Rare
	Vertigo		
	CPK increased (see special populations)		
	Impulse control (incl. pathological gambling)		

†Although very common, these adverse effects usually occur at the start of treatment only and are transient.

Further information can be found in the Summary of Product Characteristics
http://www.medicines.org.uk/emc/medicine/27412

7 Cautions

7.1 Special Populations

Hepatic Impairment
Adjustment of the dose is not necessary in patients with mild to moderate hepatic impairment. Caution is advised when treating patients with severe hepatic impairment, which may result in lower rotigotine clearance. Rotigotine has not been investigated in this patient group. A dose reduction might be needed in case of worsening of the hepatic impairment

Renal Impairment
Adjustment of the dose is not necessary in patients with mild to severe renal impairment, including those requiring dialysis. Unexpected accumulation of rotigotine levels may also occur at acute worsening of renal function

7.2 Patients undergoing cardioversion or magnetic resonance imaging

The backing layer of a rotigotine patch contains aluminium. To avoid skin burns, the patch should be removed if the patient has to undergo magnetic resonance imaging (MRI) or cardioversion.

7.3 Orthostatic hypotension

Dopamine agonists are known to impair the systemic regulation of the blood pressure resulting in postural/ orthostatic hypotension. These events have also been observed during treatment with rotigotine, but the incidence was similar to that observed in placebo-treated patients. It is recommended to monitor blood pressure, especially at the beginning of treatment.
Baseline blood pressure measurements should be taken by the specialist. The patient will be counselled on this side effect and should seek support from the GP to monitor blood pressure should they become symptomatic.

GP may refer back to the specialist if this continues to present as an issue after the initial month of treatment.
Orthostatic hypotension is screened for regularly as part of the specialist review.

7.4 Syncope

In clinical studies with rotigotine, syncope has been observed at a rate that was similar to that observed in patients treated with placebo. Because patients with clinically relevant cardiovascular disease were excluded in these studies, patients with severe cardiovascular disease should be asked about symptoms of syncope and pre-syncope.

7.5 Sudden onset of sleep and somnolence

Rotigotine has been associated with somnolence and episodes of sudden sleep onset. 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.
Prescribers should warn patients of the risk of excessive daytime sleepiness and sudden onset of sleep and of the consequent need to exercise caution when driving or operating heavy machinery.

7.6 Abnormal thinking and behaviour

Abnormal thinking and behaviour have been reported and can consist of a variety of manifestations including paranoid ideation, delusions, hallucinations, confusion, psychotic-like behaviour, disorientation, aggressive behaviour, agitation, and delirium.

7.7 Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathologic gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists, including rotigotine.
Dose reduction/tapered discontinuation should be considered if such symptoms develop.

7.8 Fibrotic complications

Cases of retroperitoneal fibrosis, pulmonary infiltrates, pleural effusion, pleural thickening, pericarditis and cardiac valvulopathy have been reported in some patients treated with ergot-derived dopaminergic agents. While these complications may resolve when treatment is discontinued, complete resolution does not always occur. Although these adverse reactions are believed to be related to the ergoline structure of these compounds, whether other, non-ergot derived dopamine agonists can cause them is unknown.

7.9 Ophthalmologic complications

Ophthalmologic monitoring is recommended at regular intervals or if vision abnormalities occur.
This should be reviewed by the hospital specialist – particularly screening for blurred vision, visual impairment or photopsia.

7.10 Heat application

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.

7.11 Application site reactions

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 direct sunlight on the area should be avoided until the skin heals. Exposure could lead to changes in the skin colour. If a generalised skin reaction (eg allergic rash, including erythematous, macular, papular rash or pruritus) associated with the use of rotigotine is observed, it should be discontinued as directed above

7.12 Dopaminergic side effects

The incidence of some dopaminergic adverse events, such as hallucinations, dyskinesia, and peripheral oedema generally is higher when given in combination with L-dopa in Parkinson's patients. This should be considered when prescribing rotigotine.

7.13 Peripheral oedema

In clinical studies in Parkinson's patients, the 6 month-specific rates of peripheral oedema remained at about 4% through the entire observation period up to 36 months

7.14 Sulphite sensitivity

Neupro contains sodium metabisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible people.

8 Contraindications

Rotigotine is contra-indicated in patients who are allergic to the active substance or to any of the excipients, including sulphite.

Initiation of dopamine agonists in general should be avoided in patients with cognitive impairment.

Further information can be found in the Summary of Product Characteristics
http://www.medicines.org.uk/emc/medicine/27412

9 Interactions

9.1 Dopamine antagonists

Because rotigotine is a dopamine agonist, it is assumed that dopamine antagonists, such as neuroleptics (eg phenothiazines, butyrophenones, thioxanthenes) or metoclopramide, may diminish the effectiveness of rotigotine, and co-administration should be avoided. Note however, that domperidone has not been shown to affect the pharmacokinetics of rotigotine.

9.2 Sedating medicines or central nervous system (CNS) depressants

Caution should be used when rotigotine is used concomitantly with other sedating medicines, eg benzodiazepines, antipsychotics, antidepressants alcohol because of possible additive effects.

9.3 Dopamine agonists

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. Co-administration of L-dopa and carbidopa with rotigotine had no effect on the pharmacokinetics of rotigotine, and rotigotine had no effect on the pharmacokinetics of L-dopa and carbidopa

Further information can be found in the Summary of Product Characteristics
http://www.medicines.org.uk/emc/medicine/27412

10 Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

The Parkinson's disease specialist team will continue to monitor efficacy, tolerability and appropriateness of Rotigotine on a 6 monthly basis, unless more frequent monitoring is required.

However, it is advisable to monitor blood pressure in patients on rotigotine patches as hypotension is a known adverse effect, especially at the beginning of therapy or after any dose increment.

11 Shared Care Responsibilities

a. Hospital specialist (Consultant and/or specialist nurse):
The decision to start rotigotine will be made by a consultant neurologist, Parkinson's or neurology specialist nurse or consultant geriatrician. Their responsibilities are as follows:

- Send a letter to the GP requesting shared care for the patient
- Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first month of treatment or until patient is stabilised)
- Perform routine follow-up on a regular basis
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring
- Evaluate any adverse events reported by the patient or the GP
- Advise the GP of the review, duration or discontinuation of treatment where appropriate
- Inform GP of patients who do not attend clinic appointments
- To provide any advice to the patient/carer or GP when requested

b. General Practitioner:

- Monitor patient's overall health and wellbeing
- Agreement to shared care guideline by the GP
- Prescribe drug treatment as directed by hospital specialist
- Help in monitoring the disease and it's management
- Report any adverse events to the hospital specialist, where appropriate
- Request advice from the hospital specialist when necessary

c. Patient or parent/carer:

- Discuss the potential benefits and side effects of treatment with the specialist and GP
- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or GP.

12 Contact numbers for advice and support

Addenbrookes Hospital NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Dr Paul Worth	Consultant Neurologist	01223 216760
Dr Duncan Forsyth	Consultant Geriatrician	01223 217785
Dr Alistair Mackett	Consultant Geriatrician	01223 217785
Nicola McQueen	Nurse Specialist	01223 349814
Ivy Smith	Nurse Specialist	01223 349814
Patients' Medicines Helpline	Medicines Information	01223 217 502

Equality and diversity statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

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Document management

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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics http://www.medicines.org.uk/emc/medicine/27412