Traffic light classification - Amber 2
Information sheet for Primary Care Prescribers

CLINICAL INFORMATION

Key points/interactions
- Nausea is a common early side effect but usually responds to domperidone (10mg tds or lowest effective dose – see MHRA advice)
- Rotigotine patches should be applied to a different site every day for 14 days.
- Dopamine agonists may cause compulsive/addictive behaviours such as gambling, compulsive shopping and hypersexuality. Patients rarely recognise such changes as side effects and rarely report them unless specifically asked.

Licensed Indications
Treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease 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 of the therapeutic effect occur (end of dose or ‘on-off’ fluctuations).

Therapeutic Summary
As per the licensed indication.

NICE recommendations for the use of rotigotine in Parkinson's disease (PD) are:

- Consider a choice of dopamine agonists, levodopa or monoamine oxidase B (MAO-B) inhibitors for people in the early stages of Parkinson's disease whose motor symptoms do not impact on their quality of life. Do not offer ergot-derived dopamine agonists as first-line treatment for Parkinson's disease.

- Offer a choice of dopamine agonists, MAO-B inhibitors or catechol-O-methyl transferase (COMT) inhibitors as an adjunct to levodopa for people with Parkinson's disease who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy, after discussing:
  - the person's individual clinical circumstances, for example, their Parkinson's disease symptoms, comorbidities and risks from polypharmacy
  - the person’s individual lifestyle circumstances, preferences, needs and goals
  - the potential benefits and harms of the different drug classes

- Choose a non-ergot-derived dopamine agonist in most cases, because of the monitoring that is needed with ergot-derived dopamine agonists. Only consider an ergot-derived dopamine agonist as an adjunct to levodopa for people with Parkinson's disease:
  - who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy and
  - whose symptoms are not adequately controlled with a non-ergot-derived dopamine agonist.
Medicines Initiation
Consultant neurologist / specialist experienced in the management of PD.

Dose Regimen

In early stage Parkinson’s disease:

- 2 mg/24 h for 2 weeks
- Increased in weekly increments of 2 mg/24 h if necessary up to a maximal dose of 8 mg/24 h
- 6-8 mg/24 h is usually a therapeutic dose.

In advanced stage Parkinson's disease:

- 4 mg/24 h for 2 weeks
- Increased in weekly increments of 2 mg/24 h if necessary up to a maximal dose of 16 mg/24 h.
- Beyond doses of 8 mg, two patches must be applied each day [and each left on for 24 hours].

Patches should be applied to clean, dry, intact healthy skin. Patches must be applied to a different site each day. Reapplication to the same site within 14 days should be avoided.

Duration of treatment
Rotigotine is a treatment for a chronic disease and therefore course length can be many years.

Contraindications
- Hypersensitivity to rotigotine or to any of the excipients
- Remove patch before MRI / cardioversion
- Pregnancy & breast feeding

Precautions
- Severe hepatic impairment
- Ophthalmological testing recommended (risk of visual disorders)- see monitoring requirements
- Avoid exposure of patch to heat
- History of dementia, confusion or hallucinations – increased risk of neuropsychiatric side effects.
- If treatment discontinuation is required, this should be done gradually. The daily dose should be reduced in steps of 2 mg/24 h with a dose reduction preferably every other day.

Monitoring
- Ask about gambling and other addictive behaviours. Patients may deny such symptoms when first asked about them.
- Ophthalmological testing recommended (risk of visual disorders)
- Blood pressure monitoring recommended, especially at the beginning of treatment.
Adverse Effects

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>Action</th>
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<tbody>
<tr>
<td>Abdominal pain, dyspepsia, constipation, dry mouth</td>
<td>Usually transient. If persists discuss with neurologist/PD nurse specialist (PDNS)</td>
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<tr>
<td>Nausea &amp; vomiting</td>
<td>Usually transient but may be quite severe. Unless very minor, prescribe Domperidone 10mg tds (or lowest effective dose - see MHRA) during dose titration; this can usually be stopped within a few weeks.</td>
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<tr>
<td>Sedation</td>
<td>Usually transient. Advise patients not to drive / operate machinery if affected. If persists discuss with neurologist.</td>
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<tr>
<td>Orthostatic hypotension</td>
<td>Usually transient. If persists discuss with neurologist/PDNS.</td>
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<tr>
<td>Light-headedness, dizziness, headache</td>
<td>Usually transient. If persists discuss with neurologist/PDNS</td>
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<tr>
<td>Palpitations, AF, SVT</td>
<td>Discuss with neurologist/PDNS</td>
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<tr>
<td>Leg oedema</td>
<td>Rarely a major problem. Discuss with neurologist if no other explanation identified</td>
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<tr>
<td>Hallucinations, confusion</td>
<td>Discuss with neurologist/PDNS</td>
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<tr>
<td>Psychotic reactions (other than hallucinations), including delusion, paranoia, delirium.</td>
<td>Discuss with neurologist/PDNS</td>
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<tr>
<td>Dopamine dysregulation syndrome - manifests as a change in behaviour, typically with an obsessional, risk-taking, sexual or financial axis.</td>
<td>Discuss with neurologist/PDNS</td>
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<tr>
<td>Hypersensitivity reactions including urticaria, rash, angioedema.</td>
<td>Discontinue and discuss with neurologist/PDNS</td>
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<tr>
<td>Visual disorders</td>
<td>Ophthalmological testing. Discuss with neurologist/PDNS</td>
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<tr>
<td>Raised hepatic enzymes</td>
<td>Discuss with neurologist/PDNS</td>
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<tr>
<td>Skin reactions</td>
<td>Ensure rotating application site. If troublesome may need to change to alternative agonist. Discuss with neurologist/PDNS</td>
</tr>
<tr>
<td>Erectile Dysfunction</td>
<td>Rarely a problem. Discuss with neurologist/PDNS</td>
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</table>

Clinically relevant medicine interactions and their management

Patients selected for treatment with Rotigotine are almost certain to be taking concomitant medications for their Parkinson's disease. In the initial stages of Rotigotine therapy the patient should be monitored for unusual side-effects or signs of potentiation of effect.

- **Neuroleptic medicinal products and other centrally acting dopamine antagonists**
  e.g. sulpiride, metoclopramide - may have an antagonistic effect if used with rotigotine. Avoid concomitant use.
- **Antihypertensives** – increased hypotensive effect
- **Memantine** - enhanced effect on dopaminergics.

For further information on contraindications, precautions, adverse effects and interactions refer to the BNF or **Summary of Product Characteristics**.

**Information given to patient**

Patients (and their family members and carers) should be given information on the following:

- The risk of excessive daytime sleepiness and sudden onset of sleep and the need to exercise caution when driving or operating machinery. If affected patients should refrain from driving or operating machinery until these effects have stopped occurring.
- The increased risk of developing impulse control disorders when taking dopamine agonist therapy, and that these may be concealed by the person affected. Advice should be given about who to contact if impulse control disorders develop.
- The risk of psychotic symptoms (hallucinations and delusions) with all Parkinson's disease treatments (and the higher risk with dopamine agonists).

**Products available**

Neupro® ▼ 1mg, 2mg, 3mg, 4mg, 6mg, 8mg patches

An estimate of the potential medicine costs (and any additional costs) to primary care

Neupro 8mg patch £150 (28 days)

**REFERENCES**

British National Formulary Jan 2018
Summary of Product Characteristics December 2017
NICE NG71 Parkinson's Disease in adults, July 2017
MHRA Drug Safety Update: Domperidone: risks of cardiac side effects, May 2014

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