CLINICAL INFORMATION

Key points/interactions
- Nausea is a common early side effect but usually responds to domperidone (20mg tds, or lowest effective dose – see MHRA advice)
- For most patients slow release preparations are more convenient to take and provide smoother symptom control
- 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 Parkinson's disease. As initial treatment as monotherapy, in order to delay the introduction of levodopa or in combination with levodopa, over the course of the disease, when the effect of levodopa wears off or becomes inconsistent and fluctuations in the therapeutic effect occur (“end of dose” or “on-off” type fluctuations).

Therapeutic Summary
As per the licensed indication.

NICE recommendations for the use of Ropinirole in Parkinson’s disease conclude that:

- Dopamine agonists may be used as a symptomatic treatment for people with early PD. (Evidence level A)
- A dopamine agonist should be titrated to a clinically efficacious dose. If side effects prevent this, another agonist or a drug from another class should be used in its place. (Evidence level D)
- In view of the monitoring required with ergot-derived dopamine agonists, a non-ergot derived agonist should be preferred in most cases. (Evidence level D)

Medicines Initiation
Consultant neurologist / specialist experience in the management of PD.

Dose Regimen
Modified Release tablets are preferred in order to avoid fluctuations in plasma levels. The usual dosing regimen is as follows:

- 2 mg MR once daily for the first week; this should be increased to 4 mg once daily from the second week of treatment
- If needed the daily dose may be increased by 2 mg at weekly or longer intervals up to a dose of 8 mg MR once daily.
- Over the next 3-5 years it is commonly necessary to gradually increase the dose to a maximum of three 8mg ropinirole MR tablets taken together once a day.
Duration of treatment
Ropinirole is a treatment for a chronic disease and therefore course length can be many years.

Contraindications
- Pregnancy and lactation
- Hypersensitivity to ropinirole or to any of the excipients
- Severe renal impairment (creatinine clearance <30 ml/min) without regular haemodialysis.
- Hepatic impairment.

Precautions
- Severe cardiovascular disease - blood pressure monitoring required, see monitoring requirements
- Pre-existing major psychotic disorders
- If it is necessary to discontinue ropinirole treatment, this should be done gradually by reducing the daily dose over the period of one week.

Monitoring
- Ask about gambling and other addictive behaviours. Patients may deny such symptoms when first asked about them.
- Blood pressure monitoring is recommended, particularly at the start of treatment, in patients with severe cardiovascular disease (in particular coronary insufficiency).

Adverse Effects

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain, dyspepsia, constipation</td>
<td>Usually transient. If persists discuss with neurologist/PD nurse specialist [PDNS]</td>
</tr>
<tr>
<td>Nausea &amp; vomiting</td>
<td>Usually transient but may be quite severe. Unless very minor, prescribe Domperidone 20mg tds (or lowest effective dose- see MHRA) during dose titration; this can usually be stopped within a few weeks.</td>
</tr>
<tr>
<td>Sedation</td>
<td>Usually transient. Advise patients not to drive / operate machinery if affected. If persists discuss with neurologist/PDNS</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>Usually transient. If persists discuss with neurologist/PDNS</td>
</tr>
<tr>
<td>Light-headedness, dizziness</td>
<td>Usually transient. If persists discuss with neurologist.</td>
</tr>
<tr>
<td>Leg oedema</td>
<td>Rarely a major problem. Discuss with neurologist if no other explanation identified</td>
</tr>
<tr>
<td>Hallucinations, confusion</td>
<td>Discuss with neurologist/PDNS</td>
</tr>
<tr>
<td>Psychotic reactions (other than hallucinations), including delusion, paranoia, delirium.</td>
<td>Discuss with neurologist/PDNS</td>
</tr>
<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>
</tr>
<tr>
<td>Hypersensitivity reactions including urticaria,</td>
<td>Discontinue and discuss with</td>
</tr>
</tbody>
</table>
Clinically relevant medicine interactions and their management
Patients selected for treatment with Ropinirole are almost certain to be taking concomitant medications for their Parkinson's disease. In the initial stages of Ropinirole 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 Ropinirole. Avoid concomitant use.
- **Inhibitors of cytochrome P450 enzyme CYP1A2** e.g. Ciprofloxacin, Fluvoxamine, Cimetidine - may lead to increased levels of ropinirole
- **Methyldopa** - antagonistic effect.
- **Memantine** - enhanced effect.
- **Oestrogens** - increased plasma concentrations of ropinirole. Dosage adjustments may be required if HRT is introduced or stopped.
- **Smoking** - may decrease ropinirole levels through CYP1A2 induction. Consider dose adjustments if patients starts or stops smoking.

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

**Information given to patient**
Patients should be warned of 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.

**Products available**
Ropinirole, ropinirole MR (as generics and Requip®, Requip XL®)

**An estimate of the number of patients affected**
100 per year

**An estimate of the potential medicine costs (and any additional costs) to primary care**
Ropinirole MR 8mg od (28 days) £42.11
Ropinirole 3mg tds (28 days) £10.38

**REFERENCES**
British National Formulary Feb 2015
Summary of Product Characteristics March 2014
NICE CG35 Parkinson’s Disease June 2006
MHRA Drug Safety Update: Domperidone: risks of cardiac side effects, May 2014

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