SHARED CARE GUIDELINE FOR TREATMENT OF PARKINSON’S DISEASE WITH APOMORPHINE

1. **Aim/Purpose of this Guideline**
   1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of apomorphine when used in Parkinson’s Disease.

2. **The Guidance**
   2.1. See below for the Shared Care Guideline.
This shared care guideline sets out details for the sharing of care of patients with Parkinson’s disease prescribed apomorphine. These guidelines provide additional limited information necessary to aid in the treatment of these patients. As with all shared care guidelines they highlight relevant prescribing issues but should be used in conjunction with relevant NICE guidance, the BNF, ABPI summary of product characteristics and do not replace them.

INTRODUCTION/BACKGROUND INFORMATION
Parkinson’s disease (PD) is a common neurodegenerative disorder with a prevalence of about 120/100,000; typical age of onset is between 50-65 years.

Motor symptoms (bradykinesia, rigidity and tremor) dominate the clinical picture. The aetiology of PD is unknown but motor symptoms are believed to be caused by a dopamine deficit in the striatum due to progressive loss of dopaminergic neurons that project to the striatum from the substantia nigra.

Drug therapy with levodopa (a precursor to dopamine) and oral dopamine agonists usually provide good symptomatic relief without significant side effects in early disease. However, after some years of treatment many patients develop motor complications which include fluctuations in motor control and dyskinesias. As the disease progresses, motor fluctuations often cause increasing disability.

Disabling motor fluctuations include unpleasant “off” periods. “Off” periods can be associated with dystonia, depression, pain, sleep dysfunction, bladder dysfunction and swallowing difficulties. With disease progression ‘off’ periods can occur suddenly rendering someone immobile in a matter of minutes. Apomorphine is a dopamine agonist, which acts directly on D1 and D2 receptors, stimulating areas of the brain where dopamine works. It produces a similar effect to levodopa, that is, the ability to prevent and reverse disabling “off” periods. However optimizing treatment can be difficult and complex for many patients.

INDICATIONS FOR THE PURPOSE OF THIS GUIDELINE
Apomorphine (as APO-go®) is licensed for use in patients with disabling motor fluctuations who are inadequately controlled with levodopa or dopamine agonists. The license covers both subcutaneous intermittent injections and continuous subcutaneous infusions. Despite its name it has no opiate or addictive properties. Apomorphine cannot be used orally because it undergoes extensive first pass metabolism to an inactive metabolite; for this reason it is administered subcutaneously.

PREPARATIONS AND DOSAGE
This shared care guideline describes the use of the APO-go brand of apomorphine, though other non-proprietary makes are available.

1. Apomorphine may be administered as a “rescue therapy” with intermittent subcutaneous bolus injections given via a prefilled APO-go® Pen to give a ‘boost’ in dopaminergic stimulation when needed. Apomorphine Pens can provide a means of rescue within 10 minutes of administration, thereby regaining mobility and independence. The effect usually lasts for about an hour. Injections are given subcutaneously either into the lower abdominal wall, below the umbilicus or in the upper outer aspects of the thighs. The injection site is rotated for each injection to avoid irritation of the skin.

2. For those patients who experience more complex motor fluctuations, including dyskinesias, a continuous subcutaneous infusion using an ambulatory APO-go® pump may be used with the APO-go® prefilled syringe.

The infusion site should be changed daily and apomorphine given during waking hours only unless there are severe night-time symptoms. Intermittent bolus boosts are also sometimes needed. The dose of apomorphine is carefully titrated on an individual basis, and can range from a few milligrams daily by intermittent subcutaneous injections, up to 100 milligrams daily by continuous infusion. In rare cases it may be necessary to give higher doses.

Products available are:

**APO-go® Pen 10mg/ml 3ml pen injector**

Usual range following initiation: 3-30mg daily in divided doses. Subcutaneous infusion may be preferable in those requiring division of injections into more than 10 doses daily.

**APO-go® PFS 5mg/ml 10ml prefilled syringe**

Usual range following initiation: 1-4mg/hour or a range of 14-60 micrograms/kg/hour

Maximum daily dose by either (or combined routes) is 100mg.

Apomorphine is prescribable on FP10 but is not available from local wholesalers, only direct from the manufacturer: Britannia Pharmaceuticals, Park View House, 65 London Road, Newbury, Berkshire, RG14 1JN (Britannia is a trading name of Genus Pharmaceuticals Ltd)

Orderline: 0844 8801326
e-mail: customers@genuspharma.com
CAUTIONS
Pulmonary or cardiovascular disease, history of postural hypotension (special care on initiation), neuropsychiatric reactions or dementia; hepatic, haemopoietic, renal, and cardiovascular monitoring on administration with levodopa; test every six months for haemolytic anaemia (development calls for specialist haematological care with dose reduction and possible discontinuation. Positive Coombs’ tests have been reported for patients receiving apomorphine and levodopa, renal impairment, pregnancy.
Patients receiving apomorphine and domperidone require an assessment of cardiac risk factors and ECG monitoring to reduce the risk of serious arrhythmia related QT-prolongation.

CONTRAINDICATIONS
Respiratory depression, hypersensitivity to apomorphine or any excipients of the medicinal product, not suitable if ‘on’ response to levodopa marred by severe dyskinesia, hypotonia or psychiatric effects, hepatic impairment, breastfeeding, not for intravenous administration.

SIDE EFFECTS
Nausea, vomiting, drowsiness (including sudden onset of sleep), confusion, hallucinations, injection-site reactions (including nodule formation) and ulceration – change injection sites in rotation; less commonly postural hypotension, breathing difficulties, dyskinesias during ‘on’ periods (may require discontinuation), haemolytic anaemia with levodopa (see Cautions), and rash; rarely eosinophilia, pathological gambling, increased libido, and hypersexuality also reported.

MONITORING

Specialist Team
- Undertake any baseline assessments including ECG
- Monitoring therapy and evaluation of adverse drug reactions
- BP monitoring (eg standing and sitting) during initiation and any dose titration phase

General Practice
- Perform a full blood count at 4-6 monthly intervals
- BP monitoring at 4-6 monthly intervals
- If patient remains on domperidone therapy long term, undertake ECG monitoring if clinically indicated (ie if a QT-prolonging or interacting drug is started or if symptoms of cardiac side effects are reported)

COMMON/SIGNIFICANT DRUG INTERACTIONS
Patients should be monitored for potential interactions during initial stages of apomorphine therapy. Particular caution should be given in patients with pre-existing cardiac disease or in patients taking vasoactive medicinal products such as antihypertensives, and especially in patients with pre-existing postural hypotension.
- Effects of apomorphine antagonized by antipsychotics
- Effects of apomorphine possibly enhanced by entacapone
- Effects of dopaminergics possibly enhanced by memantine
- Antiparkinsonian effect of dopaminergics antagonized by methyldopa

NOTES
- Prefilled syringes of apomorphine should be stored at room temperature (at or below 25ºC) and protected from light. Once opened, they should be used immediately. No antimicrobial preservative is included in the formulation so prepared syringes should be used within 24 hours. The solution must not be used if it is green or discoloured.
- APO-go Pens should be stored in a cool dry place, but not in a fridge and discarded 48hrs after opening.
- APO-go stains green on contact so care should be taken to avoid spillages. Lemon juice may prevent green colouring from developing if used immediately. Bleach may help reduce stains on kitchen surfaces.

REFERENCES
- SPC: APO-go PFS 5mg/ml
- SPC: APO-go Pens 10mg/ml
  http://emc.medicines.org.uk/medicine/12941/SPC/APO-go+Pen+10mg+ml+Solution+for+Injection/
- APO-go information for both patients and healthcare professionals
  http://www.apo-go.co.uk/
- 24/7 Helpline manned by APO-go advisers: 0844 8801327

Request for other formats
Please ask if you would like to receive this leaflet in large print, braille, on CD or in any other languages. If you would like the leaflet in an alternative format please contact the NHS Kernow Communications Team at communications@kernowccg.nhs.uk or call 01726 627800
AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of adult patients who are prescribed apomorphine can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

In its guidelines on responsibility for prescribing (circular EL(91)127) between hospitals and GPs, the DH has advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

Specialist Team

- Patient selection and conduct any necessary baseline assessments to determine suitability.
- Agreement to initiate treatment reached between patient, GP and Specialist Team (under Shared Care Guideline)
- Liaison (including provision of information) with patient, spouse, carers and Primary Care Teams.
- Start domperidone 10 mg** three times daily three days prior to apomorphine challenge (See Appendix 1 for Challenge instructions) and arrange day case admission for apomorphine challenge. **For adult patients a dose of 10mg TDS is used however there are some patients who may require 20mgs TDS which will be reduced to lowest effective dose as soon as possible. Domperidone is contraindicated in people with underlying cardiac conditions and other risk factors, including those who take concomitant medication known to cause QT prolongation or potent CYP3A4 inhibitors (such as ketoconazole and erythromycin); and in people with severe hepatic impairment. Once apomorphine treatment is established, the domperidone dose should be gradually reduced to the lowest effective dose.
- Specialist team to initiate either intermittent apomorphine injection or continuous infusion driver and optimise anti-parkinsonian drug therapy.
- Monitoring and evaluation of adverse drug reactions.
- Telephone contact for patients, carers and health professionals, providing the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.
- The Consultant / Specialist Team will be responsible for disease and drug response monitoring; this will be undertaken in the outpatient setting, and where necessary, the patient’s home.
- Discontinue treatment when considered to be no longer efficacious or if side-effects outweigh benefit.
- Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- Prompt communication with GP of any changes in treatment or dose requirements, results of monitoring undertaken and assessment of adverse events.
- The Specialist Team will inform the relevant community pharmacy / dispensing surgery of supply arrangements for apomorphine and consumables.

Responsibilities of GP

- Reply to request for shared care as soon as practical.
- To inform the specialist team of any significant developments, or deterioration, such as the occurrence of side effects or an inability to administer apomorphine.
- Be aware that domperidone may be associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death, and hence is contraindicated in those with underlying cardiac conditions and other risk factors.
- Perform a full blood count at 4-6 monthly intervals.
- BP monitoring at 4-6 monthly intervals.
- For patients remaining on domperidone therapy long term, ECG monitoring if clinically indicated.
- Following initiation to prescribe on-going drug therapy as recommended by the specialist team, unless Homecare Service is initiated.
- To facilitate the co-ordination of on-going patient care within the community and home environment, liaising with the Specialist Team when necessary.

Patient: and carer responsibilities

- Report any adverse effects to their GP and/or specialist regarding their treatment. Patients should specifically report if they experience a racing heartbeat, palpitations, dizziness, fainting, or black outs.
- Ensure that they have a clear understanding of their treatment and they attend for monitoring requirements as per shared care guideline.
- Take prescriptions to the pharmacy / dispensing surgery as soon as possible so they have adequate time to obtain supplies of the medicine.

BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE PARKINSON’S TEAM AND RELEVANT APO-GO SUPPORT ROUTES
Appendix 1: Apomorphine Challenge

Before therapy can be initiated an apomorphine challenge is necessary in order to:
1. Determine whether a patient has a positive response to the medication
2. Establish the optimum dose for the individual patient
3. Observe the patient for side effects such as nausea, vomiting, postural hypotension, hallucinations and sleepiness.

Three days prior to and throughout the challenge, domperidone 10mg** orally TDS is commenced (usually at home) to avert the significant emetic effects of apomorphine. Exceptionally a higher dose of domperidone 20mg TDS may be used). The challenge is usually performed as a day case in a safe clinical environment with medical support.

Procedure

1. Obtain a starter pack of 5 APO-go Pens. This is available free of charge from Britannia Pharmaceuticals for the challenge procedure
2. Pre-treat with domperidone 10mg TDS** (exceptionally a higher dose of 20mg TDS may be used) for 72 hours prior to and ongoing following a positive outcome of the challenge. The dosage may then be titrated downwards as tolerance develops.
3. Patients should obtain a prescription from their GP. The patient should not receive any oral anti-Parkinson medication for a minimum of eight hours prior to the challenge, unless necessary in order to provoke an “off” state. The patient’s mobility should be considered if the challenge is to be performed as a day case. If necessary for mobility a dose of medication such as co-benaldopa dispersible 62.5mg may be required.
4. Motor function is assessed at baseline using the Unified Parkinson’s Disease Rating Scale (UPDRS) section III Motor Function, together with a timed a 12 (if practicable) metre walk (the time it takes the patient to rise from a chair with arms folded then walk 6m, turn, return 6m, then sit down). Lying and standing blood pressure is also recorded due to the possible hypotensive effects of dopamine agonists. These assessments are repeated after sequential doses of apomorphine.
5. Administer 1mg apomorphine subcutaneously as a test dose and repeat above motor assessment and blood pressure 20-30 minutes following dose, monitor for side effects and observe for a positive response.
6. If there is no or a poor response, give a subsequent dose of 2-3 mg apomorphine. Continue to assess as above and observe.
7. Increase the dose in incremental steps every 45-60 minutes (eg. 2mg, 3mg, 5mg, 7mg) Stop when a positive response is seen. If at 7mg there is no response, then the patient is termed a non-responder. If a mild response is noted at 7mg, discuss with the patient’s neurologist as to whether then the maximum dose of 10mg should be administered.

A challenge is positive if either the following are seen, for example:
1. A decrease in UPDRS motor score by at least 20%.
2. A minimum of 20% improvement in timed walking.

Supply arrangements
The apomorphine (APO-go) syringes are supplied by the company free of charge for the challenge tests. It is good practice to record the batch no of the syringes used together with the expiry dates against the patient name preferably on the prescription chart. Pharmacy will also have a note of receipt and will store the syringes until needed.

** Note recent MHRA safety warnings with domperidone. See ‘Specialist Team Responsibilities’ above
3. Monitoring compliance and effectiveness

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<th>Compliance with prescribing and administration in accordance with this guideline (or other safe practice)</th>
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<td>Tool</td>
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<td>Acting on recommendations and Lead(s)</td>
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<tr>
<td>Change in practice and lessons to be shared</td>
<td>Relevant Clinical Staff</td>
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4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the ‘Equality, Diversity & Human Rights Policy’ or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.
### Appendix 1. Governance Information

<table>
<thead>
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<th>Shared care Guideline for Treatment of Parkinson’s Disease with Apomorphine</th>
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<td>May 2016</td>
</tr>
<tr>
<td>Date Valid From:</td>
<td>May 2016</td>
</tr>
<tr>
<td>Date Valid To:</td>
<td>June 2019</td>
</tr>
<tr>
<td>Directorate / Department responsible (author/owner):</td>
<td>M Wilcock, Head of Prescribing Support Unit, Pharmacy Department, RCHT</td>
</tr>
<tr>
<td>Contact details:</td>
<td>01872 253548</td>
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<tr>
<td>Brief summary of contents</td>
<td>Some clinical issues and details of prescribing responsibilities for GP and specialists</td>
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<td>Medical Director</td>
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<tr>
<td>Date revised:</td>
<td>May 2016</td>
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<tr>
<td>This document replaces (exact title of previous version):</td>
<td>Treatment of Parkinson’s Disease with Apomorphine shared care guideline v2.0</td>
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<td>Approval route (names of committees)/consultation:</td>
<td>Cornwall Area Prescribing Committee</td>
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<tr>
<td>Divisional Manager confirming approval processes</td>
<td>Karen Jarvill, Associate Director CSCS</td>
</tr>
<tr>
<td>Name and Post Title of additional signatories</td>
<td>Janet Gardner, Governance Lead CSCS</td>
</tr>
<tr>
<td>Signature of Executive Director giving approval</td>
<td>{Original Copy Signed}</td>
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<tr>
<td>Publication Location (refer to Policy on Policies – Approvals and Ratification):</td>
<td>Internet &amp; Intranet</td>
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<td>Clinical / Pharmacy</td>
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<td>Training Need Identified?</td>
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## Version Control Table

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<th>Version No</th>
<th>Summary of Changes</th>
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<td>V1.0</td>
<td></td>
<td>M Wilcock, Head of Prescribing Support Unit</td>
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<tr>
<td>Sept 2014</td>
<td>V2.0</td>
<td>Update warning for domperidone</td>
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<tr>
<td>May 2016</td>
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<td>ECG monitoring advice included</td>
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**All or part of this document can be released under the Freedom of Information Act 2000**

**This document is to be retained for 10 years from the date of expiry.**

**This document is only valid on the day of printing**

**Controlled Document**

This document has been created following the Royal Cornwall Hospitals NHS Trust Policy on Document Production. It should not be altered in any way without the express permission of the author or their Line Manager.
## Appendix 2. Initial Equality Impact Assessment Form

<table>
<thead>
<tr>
<th>Name of the strategy / policy / proposal / service function to be assessed (hereafter referred to as <strong>policy</strong>) <em>(Provide brief description):</em></th>
<th>Shared care Guideline for Treatment of Parkinson’s Disease with Apomorphine</th>
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<tr>
<td>Directorate and service area: Pharmacy</td>
<td>Is this a new or existing Policy?</td>
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<td></td>
<td>Existing</td>
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<tr>
<td>Name of individual completing assessment: Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td>
<td>Telephone: 01726 627953</td>
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### 1. Policy Aim*

**Who is the strategy / policy / proposal / service function aimed at?**

- To provide information on prescribing of apomorphine to enable General Practitioners to take over prescribing responsibility from secondary care.

### 2. Policy Objectives*

- To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)

### 3. Policy – intended Outcomes*

- Confident and competent prescribers, enabling medicines to be access in a primary care setting.

### 4. *How will you measure the outcome?*

- Six monthly review

### 5. Who is intended to benefit from the policy?

- General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.

### 6a) Is consultation required with the workforce, equality groups, local interest groups etc. around this policy?

- no

### 6b) If yes, have these *groups been consulted?*

### 6c) Please list any groups who have been consulted about this procedure.

### 7. The Impact

Please complete the following table.

<table>
<thead>
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<th>Equality Strands:</th>
<th>Yes</th>
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<th>Rationale for Assessment / Existing Evidence</th>
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<td>Age</td>
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You will need to continue to a full Equality Impact Assessment if the following have been highlighted:
- You have ticked “Yes” in any column above and
- No consultation or evidence of there being consultation- this excludes any policies which have been identified as not requiring consultation. **or**
- Major service redesign or development

8. Please indicate if a full equality analysis is recommended. **No**

9. If you are not recommending a Full Impact assessment please explain why.

<table>
<thead>
<tr>
<th><strong>Signature of policy developer / lead manager / director</strong></th>
<th><strong>Date of completion and submission</strong></th>
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<tr>
<th><strong>Names and signatures of members carrying out the Screening Assessment</strong></th>
<th><strong>1. Dan Thomas</strong></th>
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<tbody>
<tr>
<td></td>
<td><strong>2. Mike Wilcock</strong></td>
</tr>
</tbody>
</table>

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead, c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

A summary of the results will be published on the Trust’s web site.

Signed __________________

Date __________________