Shared care guidelines

Apomorphine injection — Idiopathic Parkinson's disease

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).
This guideline reinforces the basic premise that:
When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the "sharing of information with the individual GP and their mutual agreement to the transfer of care."
These are not rigid guidelines. In all cases, Consultants and GPs should discuss the appropriate management of individual patients. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Indications: Treatment of motor fluctuations ('on-off' phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication. Apomorphine may be administered as a "rescue therapy" with intermittent subcutaneous bolus injections given via a prefilled APO-go Pen. Patients selected for treatment with intermittent apomorphine should be able to recognise the onset of their 'off' symptoms and be capable of injecting themselves or have a responsible carer able to inject for them when required. For those patients who experience more complex motor fluctuations, including dyskinesias, a continuous subcutaneous infusion using an ambulatory APO-go pump may be used.	**Dosage and administration:** The optimal dosage of apomorphine has to be determined on an individual patient basis and the threshold dose is determined by the specialist using incremental dosing schedules. **Intermittent injection** – typically 1-10 injections per day, each dose no more than 10mg **Continuous infusion** - typically 1–6 mg per hour (but may be higher, dependent upon individual response), mostly during waking hours but may be necessary for overnight infusion according to patients needs. 24 hour infusions are not recommended. Usual dose = 3 to 30mg, by subcutaneous injection, daily in divided doses Maximum daily dose = 100mg

Monitoring requirements:
Monitor FBC, Coombs test, LFT, U&Es, ESR, BP and cardiovascular function via ECG to exclude cardiac conduction problems or significant cardiac disease. FBC, LFT, U&Es, ESR, Coombs and BP should be monitored 6 monthly in movement disorder clinic.
ECG is required as apomorphine at higher doses can cause QT prolongation. When used in conjunction with domperidone this effect can be exacerbated. Domperidone is used when initiating apomorphine to prevent side effects of nausea and vomiting.

Additional information:
Apomorphine is a dopamine agonist, which acts directly on D_1 and D_2 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. Despite its name **it has no opiate or addictive properties**. Apomorphine cannot be used orally because it undergoes extensive first pass metabolism (in the liver) to an inactive metabolite; for this reason it is administered subcutaneously.

Apomorphine Consumables:
Genus pharmaceuticals will loan the Apo-Go apomorphine pump and syringes free of charge to the hospital consultant for use by the patient. Patients will need to sign a patient agreement form. The information is used to track pumps and ensure patients receive a regular supply of syringes and connectors.
Apomorphine pre-filled syringes and apomorphine intermittent injection pens can be prescribed on an FP10.
An APO-go Helpline is available for patients and healthcare professionals 24/7, 365 days a year: 08448801327.
Replacement pumps can be dispatched for delivery within hours in the event of an emergency.

Contraindications: Apomorphine should not be given to children and adolescents under 18 years of age, patients with respiratory depression, dementia, psychotic diseases, hepatic insufficiency, and hypersensitivity to apomorphine or any excipients of the medicinal product. Apomorphine must not be administered to patients who have an 'on' response to levodopa which is marred by severe dyskinesia or dystonia.

Drug interactions:
The possible effects of apomorphine on the plasma concentrations of other drugs have not been studied. Therefore caution is advised when combining apomorphine with other medicinal products, especially those with a narrow therapeutic range. Neuroleptic medicinal products may have an antagonistic effect if used with apomorphine. There is a potential interaction

Principal author: Geraldine McKerrel
(Lead DME Pharmacist, WUTH)
Updated by: Craig McCallum
(Senior DME Pharmacist, WUTH)

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between clozapine and apomorphine, however clozapine may also be used to reduce the symptoms of neuropsychiatric complications under specialist care.
It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval. *Examples being*: Amiodarone, astemizole, chlorpromazine, cisapride, citalopram, clarithromycin, disopyramide, erythromycin, flecainide, haloperidol, moxifloxacin, pentamidine, procainamide, quinidine and sotalol. This list is not exhaustive, see BNF for full details.

Cautions: Prior to initiating apomorphine patients should receive 3 days treatment with domperidone at a dose of 10 mg TDS to prevent drug induced nausea and vomiting. In 2014 the MHRA released a safety warning highlighting that domperidone may be associated with a small increased risk of serious ventricular arrhythmia or sudden cardiac death as it can prolong the QT interval. These risks may be higher in patients who are over 60 and in patients who receive an oral daily dose of over 30mg. For this reason domperidone should be used at the lowest effective dose for the shortest required time. If high risk consider cyclizine (ondansetron can compound hypotension when given with Apomorphine and is not advised).

Adverse effects and action to be taken if abnormal results/adverse effects:

Adverse event System – symptom/sign	**Action to be taken**	**By whom**
Localised discomfort at needle site	Rotate injection site daily	Patient / carer / district nurses
Nodules formation at needle or infusion site. Usually asymptomatic but may persist in patients on high doses. Severe nodule formation may lead to worsening of symptoms due to erratic absorption of Apomorphine	Rotate injection site. Massage to injection sites is recognised to reduce nodule formation. Ultrasound therapy has been anecdotally been said to alleviate severe nodule formation	Patient / carer / district nurses
Nausea & vomiting. Usually transient and resolved within 6-8 weeks	Treatment with domperidone (typical dosage 10mg three times a day) before and during apomorphine HCl therapy is essential. Once treatment has been established domperidone therapy may be gradually reduced and can be successfully discontinued in most patients within 6-8 weeks	GP as advised by Consultant / Parkinson's disease nurse specialist (PDNS)
Allergic reactions including bronchospasm and anaphylaxis (due to sodium bisulphate)	Withhold and discuss with Consultant/PDNS	GP
Light-headedness	Discuss with Consultant /PDNS	GP
Postural hypotension is seen infrequently and is usually transient	Care should be exercised in patients with pre-existing cardiac disease or in patients taking vasoactive medicinal products such as antihypertensives, and in patients with pre-existing postural hypotension. Discuss with Consultant /PDNS if persistent or causing falls.	GP
Dyskinesias during 'On' periods	Discuss with Consultant /PDNS	GP
Coomb's positive haemolytic anaemia	Discuss with Consultant /PDNS. Coombs test every 6 months, if positive, frequent FBCs required. May need to refer to haematologist	GP
Eosinophilia in up to 10% of patients	Discuss with Consultant /PDNS	GP
Neuropsychiatric complications – hallucinations, euphoria, increased libido, confusion, personality changes, agitation, restlessness, psychosis, sleep disturbances	Discuss with Consultant /PDNS	GP
Sedation. Usually transient	Advise patients not to drive / operate machinery if affected. If persists discuss with Consultant / PDNS	GP

Specialist responsibilities (Consultant /PDNS):
Diagnose condition and discuss with patient the benefits and side effects of treatment with apomorphine
Perform apomorphine challenge
Monitor FBC, Coombs test, LFT, U&Es, ESR, BP and cardiovascular function via ECG to exclude cardiac conduction problems or significant cardiac disease upon initiation of apomorphine.
FBC, LFT, U&Es, ESR, Coombs and BP should be monitored 6 monthly in movement disorder clinic.
Ongoing ECG monitoring is not required unless apomorphine dose is increased or if domperidone doses are increased or added in. In these cases it is the responsibility of the specialist consultant to carry out repeat ECG monitoring.
Request prescriptions for the correct form of apomorphine from the GP
Review patient regularly and titrate apomorphine dose as appropriate
Communicate promptly with GP when treatment is changed
Advise GPs when to refer back and when and how to stop treatment
Report adverse events to the CSM.
Ensure clear backup arrangements exist for GPs, for advice and support.

GP's responsibilities:
Provide prescription for domperidone prior to apomorphine challenge, domperidone can be reviewed and usually withdrawn after 6-8 weeks, depending on symptoms.
Continue to provide prescriptions for correct form of apomorpine (ampoules, pre-filled syringes, pre-filled pens) every month
Monitor FBC, LFTs, U&Es, ESR and BP 6 monthly if the patient is in the community and unable to continue to attend clinic with the PD specialist consultant. This will routinely be monitored in movement disorder clinic as above.
Write patient medicines administration chart if required for district nurses to administer apomorphine via the apo-go pump. This should include the following details:

- Name of patient and date of birth and NHS number if available
- Name and signature of authorised prescriber
- Date prescribed
- Number of milligrams of apomorphine to be infused **per hour** and length of infusion e.g. 12 or 15 hours
- Name and strength of medicine (apomorphine e.g. 50mg in 10ml prefilled syringe)
- Route (subcutaneous infusion)
- Frequency of infusion e.g. daily

Patient's responsibilities:
Report to the specialist or GP if he or she does not have a clear understanding of the treatment or has concerns in relation to treatment with apomorphine
Report any adverse effects to the GP or specialist whilst taking apomorphine

Secondary care review:
Every six months in movement disorder clinic. Where there is a specific problem, patient may be seen in the community by the Parkinsons disease nurse specialist (if appropriate) or return earlier to clinic for review.

Availability:
Apomorphine pre-filled pens 10mg/ml – 3ml pens: MIMS December 2015, price £123.91 for 5 pens
Apomorphine pre-filled syringes 5mg/ml - 50mg in 10ml: MIMS December 2015, price £73.11 for 5 syringes

Back up advice and support:	**Telephone**
Parkinson's disease specialist nurse Dr M O'Neill Apo-go Helpline	0151 643 5330 Secretary: 0151 604 7445 0844 880 1327

Principal author	Geraldine McKerrell (Lead DME Pharmacist WUTH)
Amendments by:	Craig McCallum (Senior DME Pharmacist WUTH)
Reviewed by:	Helen Dingle, Prescribing Adviser, Midlands and Lancashire Commissioning Support Unit (MLCSU) on behalf of Wirral CCG Dr M O'Neill, Consultant in Elderly Medicine, WUTH