Apomorphine

Neurology shared care guideline

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

Licensed indications: treatment of disabling motor fluctuations ('on-off' phenomena) in patients with Parkinson's disease which persist despite individually titrated treatment with levodopa (with a peripheral decarboxylase inhibitor) and/or other dopamine agonists.

Unlicensed indications: may also be considered in those with Parkinson's disease who are nil by mouth and unable to take medications by an alternative route

The first dose of apomorphine should be administered in the controlled environment of a specialist movement disorders clinic. The patient should be supervised by a physician experienced in the treatment of complex Parkinson's disease (e.g. subspecialist neurologist / movement disorders specialist).

Despite its name, apomorphine has no opiate or addictive properties.

Adult dosage and administration

The patient's treatment with levodopa, with or without dopamine agonists, should be optimised before starting apomorphine. The patient must also be established on domperidone (ensure MHRA safety advice regarding domperidone is followed), usually 10mg three times daily for at least two days prior to initiation of therapy. Higher doses of domperidone may be needed but the lowest effective dose should be used for the shortest possible duration.

Apomorphine must not be used via the intravenous route. Usual range (after initiation in hospital): 3 – 30mg daily by subcutaneous injection in divided doses. The maximum single dose is 10mg, the maximum daily dose is 100mg.

For patients requiring division of dose into more than about 4 – 10 injections daily, continuous subcutaneous infusions are used (during waking hours only) at a usual rate of 1 – 4mg/hour with the site being changed daily.

Available as:

Preparations for intermittent administration:

Injection: apomorphine hydrochloride 10mg/ml injection, 2ml and 5ml amp;

Pen injector: apomorphine hydrochloride 10mg/ml, 3ml

Preparations for continuous infusion:

Pre-filled syringe: apomorphine hydrochloride 5mg/ml solution for infusion 10ml; infused by minipump or syringe-driver.

Hospital specialist responsibilities

- Assess patient is suitable for treatment:
  - exclude cardiac conduction problems (QTc prolongation is of particular concern) or significant cardiac disease via ECG.
  - review patient's medication history to exclude other unnecessary medications that could cause QTc prolongation and for other potential significant interactions with the new treatment. Discuss with GP if any concerns.
  - exclude hepatic impairment.
- Arrange for administration of first dose of apomorphine at a movement disorders specialist clinic, and the re-establishment of any other antiparkinsonian drugs.
- Liaise with the Parkinson's disease nurse specialist / apomorphine nurse specialist to provide training for patient, carer and other healthcare professionals involved in the administration of apomorphine and liaison with community nursing service as appropriate.
- The patient's Parkinson's disease nurse specialist will be made aware of the initiation of apomorphine therapy and the appropriate prescription.
- Arrange shared care with the patient's GP.
- Provide the GP with information relating to preparations, needles and giving sets to be prescribed.
- Provide patient / carer with relevant written information on use, side-effects and need for monitoring of medication.
- Undertake baseline tests:
  - **FBC**
  - **U&E**
- Review results of safety monitoring and request additional tests as required eg. Coombs' test at review appointments.
- Advise on apomorphine dosage adjustments (for continuous infusion this may take several months) and withdrawal of domperidone.
- Have in place a system to manage pump failure should this occur.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.

GP responsibilities

- Prescribe apomorphine and needles as advised by the specialist.
- Arrange and record ongoing monitoring as agreed with specialist:
  - **FBC** and **reticulocytes** every 4-6 months. If test results are abnormal, consult with Parkinson's disease nurse specialist
- Consult promptly with the Parkinson's disease nurse specialist if the patient deteriorates or has problems administering apomorphine
- If patient is not compliant with monitoring, liaise with the Parkinson's disease nurse specialist regarding the appropriateness of ongoing prescription, or if an alternate regimen and management strategy is required.
- Gradual withdrawal of domperidone as advised by secondary care
- Inform the Parkinson's disease nurse specialist immediately if impulse control disorders develop (pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating)
- Report any adverse drug reactions to the Parkinson's disease nurse specialist and usual bodies (eg. MHRA / CHM).
- Ensure no significant drug interactions with other medicines.

Action required in event of monitoring abnormalities

Test	Results	Action Required
Platelets	Less than 120 x 10^9/L	Continue treatment and contact Parkinson's disease nurse specialist and apomorphine nurse advisor.
Haemoglobin	below normal range for age from local laboratory without another obvious cause	
Reticulocytes	Greater than 100 x 10^9/L or > 2.5%	

Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values, specialist will advise.

Adverse effects, precautions and contraindications

Common adverse effects are: confusion, hallucinations, dizziness/light-headedness and yawning. Nausea and vomiting is also common, particularly at the onset of treatment (addition of domperidone may be advised). If these common side effects are persistent or severe they should be reported to the Parkinson's disease nurse specialist.

Sudden onset of sleep: excessive daytime sleepiness and sudden onset of sleep can occur with dopamine agonists necessitating appropriate advice on driving.

Injection site reactions are common - change injection sites in rotation. If subcutaneous nodules develop, liaise with the Parkinson's disease nurse specialist.

Haemolytic anaemia and thrombocytopenia have been reported: refer to the Parkinson's disease nurse specialist.

Postural hypotension: is transitory and should not persist after discharge from hospital. Caution should be exercised if it is co-administered with antihypertensive agents. Consider reviewing antihypertensives pre/post introduction of apomorphine as some patients no longer need them.

A symptom complex resembling the neuroleptic malignant syndrome (NMS) (characterised by elevated temperature, muscular rigidity, altered consciousness and autonomic instability), with no other obvious aetiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in antiparkinson therapy. If NMS is suspected the patient should be referred to the Parkinson's disease nurse specialist urgently.

Impulse control disorders: patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including apomorphine hydrochloride. Dose reduction/tapered discontinuation should be considered if such symptoms develop.

Pregnancy: apomorphine should not be used in pregnancy unless clearly necessary.

Breastfeeding: a decision on whether to continue/discontinue breastfeeding or to continue/discontinue therapy with apomorphine should be made taking into account the benefit of breast-feeding to the child and the benefit of APO-go to the woman.

Contraindications include:
Patients with respiratory depression, dementia, psychotic diseases, hepatic insufficiency or hypersensitivity to the active substance or to any of the excipients
Intermittent apomorphine treatment is not suitable for patients who have an 'on' response to levodopa that is marred by severe dyskinesia or dystonia.

Common drug interactions

- **Antipsychotics**: effects of apomorphine are antagonised by antipsychotics.
- **Memantine**: effects of dopaminergics possibly enhanced by memantine.
- **Methyldopa**: antiparkinsonian effects of apomorphine are antagonised by methyldopa.
- **Ondansetron ($5HT_3$ antagonists):** possible increased hypotensive effect, avoid concomitant use.
- Avoid the administration of apomorphine with other drugs known to prolong the QT interval.
- Antihypertensive and vasoactive medicines: apomorphine may increase the antihypertensive effects of these medicinal products.

Communication

For any queries relating to this patient's treatment with apomorphine, please contact the patient's Parkinson's disease nurse / nursing contact named below:

Name: _____

Location: _____

Tel: _____

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC at www.medicines.org.uk or the BNF

Date Prepared: June 2023 Date of review: June 2028