This guideline provides prescribing and monitoring guidance for apomorphine therapy. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the BNF.

BACKGROUND FOR USE
Apomorphine is a hospital only drug and is red on the Bucks traffic light list. It may only be prescribed by Buckinghamshire Healthcare NHS Trust (BHNHST) Consultant Neurologists in patients who are diagnosed with Parkinson’s disease (PD), who:
- Experience disabling motor fluctuations despite optimal oral therapy.
- Have no pre-existing neuropsychiatric symptoms including impulse control disorder.
- Have no symptoms of respiratory depression, hypersensitivity to opioids or dementia.

SUPPORTING INFORMATION
Disabling motor fluctuations are a common complication of idiopathic PD treated with levodopa. Some of these patients will benefit from the use of apomorphine.

Apomorphine is a directly acting dopamine agonist with no opiate or addictive properties. Apomorphine is not used orally because it undergoes extensive first pass metabolism to an inactive metabolite. Treatment with apomorphine is usually either by intermittent subcutaneous (s/c) injection or continuous s/c infusion. Following a single s/c dose, apomorphine has an onset of action of between 4 - 12 minutes. The effect lasts between 40 - 60 minutes.

The aim of treatment is to optimise the delicate balance between optimal response and minimal side effects.

**Intermittent subcutaneous injection**
Each dose should be administered as an s/c injection in the thigh or abdomen using a multi-dose disposable pen injector. Alternatively, the required dose can be drawn up and administered using an insulin syringe.

**Subcutaneous infusion**
Administered using an APO-go® PFS 5 mg/ml pre-filled syringe via an APO-go® pump. Alternatively, a 5 ml ampoule (10 mg/ml) can be diluted with 5 ml sterile sodium chloride 0.9% to make a 5 mg/ml solution for delivery via a Graseby™ or APO-go® pump.

The injection site should be covered using a suitable dressing, e.g. Tegaderm™ 6 cm x 7 cm. To minimise local irritation the site of administration should be rotated daily.

APO-go® pumps are available on permanent loan.

**Preparations available**
- APO-go® ampoules 10 mg/ml solution for injection (2 ml and 5 ml).
- APO-go® pen 10 mg/ml solution for injection (3 ml disposable multiple-dose pen injector).
- APO-go® PFS 5 mg/ml solution for infusion (10 ml pre-filled syringe).

**Equipment required**
All forms of apomorphine are available on prescription.

The APO-go® pump is available on loan from Genus Pharmaceuticals (formerly Britannia). The company also supply the syringe driver syringes and connectors.

Tegaderm™ dressings are ordered by the District Nurses.

Neria™ G29 10 mm 60 cm lines, available on prescription.
Patient information

Before agreeing to apomorphine therapy, patients and their carers should be fully informed about what is involved. This can be done through discussion, provision of literature and visual aids such as DVDs. This should be documented in the patient’s clinical records.

Patients must be informed that apomorphine may be associated with somnolence and advised to exercise caution while driving or operating machines during treatment with apomorphine. Patients who have experienced somnolence should be counselled to refrain from driving or operating machines.

RESPONSIBILITIES

Consultant Neurologist and Parkinson’s Disease Nurse Specialist (PDNS)

1. Assess the suitability of patients for treatment with apomorphine.
2. Baseline measurements of blood count, urea, creatinine and liver function tests, blood pressure and ECG measurement before therapy initiated.
3. Liaise with district nurses as necessary.
4. Prescribe apomorphine.
5. Ensure patient has the necessary equipment.
6. Follow up visits and clinic appointments as necessary minimum 3 – 6 months by PDNS or Consultant Neurologist.
7. Check full blood count, urea, creatinine and liver function tests, blood pressure and heart rate measurement every 6 months.
8. Review and evaluate test results and any adverse drug reactions.
9. Liaise with GP regarding changes in disease management, drug dose and missed clinic appointments (for information).
10. Ensure the patient understands the nature and complications of drug therapy and their role in reporting adverse effects promptly.
11. Be available to give advice to GP and patient.
12. Monitor and evaluate response to anti-Parkinson’s therapy and initiate changes as necessary.
13. Be responsible for training patients, carers and other health professionals in subcutaneous administration of apomorphine, either as intermittent injections or continuous infusion.

Pharmacy duration of supply

Patients can opt for home delivery of apomorphine. Under these circumstances the prescription can be generated by the specialist team but authorised by BHNHST Pharmacy. If patients choose not to have home delivery, they can collect their prescription from the hospital pharmacy.

CONTRAINDICATIONS AND PRECAUTIONS

Contraindications

Apomorphine is contraindicated in patients with any respiratory depression, dementia, psychotic diseases or hepatic insufficiency. Apomorphine should not be administered to anyone with a known hypersensitivity to apomorphine or any of its excipients.

Pharmaceutical precautions

All forms of apomorphine should be stored at room temperature (no greater than 25°C) and protected from light.

The solution should be inspected visually prior to use. Only clear, colourless and particle free solution should be used.

Solution for injection which has turned green should be discarded.

APO-go® pens have a 48 hour expiry once in use.

PFS syringes should be discarded within 24 hours once in use.

Syringes filled with apomorphine from ampoules should be stored in the fridge if not for immediate use and should be discarded within 24 hours of preparation.
Pregnancy and lactation

There is no experience of apomorphine usage in pregnant women. Animal reproduction studies do not indicate any teratogenic effects, but doses given to rats which are toxic to the mother can lead to a failure to breathe in the newborn. The potential risk for humans is unknown.

APO-go® should not be used in pregnancy unless clearly necessary.

It is not known whether apomorphine is excreted in breast milk. A decision on whether to continue/discontinue breastfeeding or to continue/discontinue therapy should be made taking into account the benefit of breastfeeding to the child and the benefit to apomorphine to the woman.

DOSAGE AND ADMINISTRATION

Premedication with oral domperidone, 20 mg three times a day, starting 72 hours before initiation of therapy is essential.

The dose will be determined on an individual patient basis during an apomorphine challenge test. Individual bolus injections should not exceed 10 mg. The typical range for intermittent injections is between 3 - 30 mg daily. The total daily dose of apomorphine, by either route, should not exceed 100 mg daily.

TIME TO RESPONSE

Motor function is assessed with the patient switched off at baseline, then 1.5 mg apomorphine is given and the patient’s motor response is observed for up to 30 minutes. If there is no response a subsequent dose of 3 mg is given and the motor response is observed, the dose is increased incrementally every 30 minutes until a response is seen (i.e. 1.5 mg, 3 mg, 5 mg, 7 mg). If no response at 7 mg is observed the patient is considered a non-responder. If a mild response is noted at 7 mg then a final maximum dose of 10 mg can be given to clarify the effect.

Motor function is assessed using the Unified Parkinson’s Disease Rating Scale (UPDRS) at baseline and then 20 – 30 minutes after each dose of apomorphine, in addition the time it takes a patient to rise from a chair with arms folded and walk 12 metres can be used as measure of response. An improvement of 15 - 20% on the UPDRS score and a 25% improvement in walking time is judged to be a positive result.

PRE-TREATMENT ASSESSMENT BY THE SPECIALIST

Baseline measurements of blood count, urea, creatinine and liver function tests, blood pressure and ECG measurement before therapy initiated.

Identification of suitable patients for apomorphine therapy: Patients with motor fluctuations leading to increased difficulties with daily living, increased disability and increased dependence on others. This includes patients with motor fluctuations such as “off” periods, painful off dystonia and peak dose or biphasic dyskinesia.

ONGOING MONITORING BY THE SPECIALIST

Periodic clinical evaluation and monitoring of hepatic, renal and cardiovascular function is advised every 6 – 12 months.

All patients with PD are reviewed every 6 months either by the Neurologist or PDNS. During the apomorphine initiation period, the patient will be regularly monitored by the PDNS, daily during the first week and then as necessary with the patient’s agreement but at least every 4 – 8 weeks during the first 3 months.
SIDE EFFECTS AND ACTIONS TO BE TAKEN

Adverse effects

Apomorphine is a potent emetic. Tolerance to this effect develops over time, allowing eventual withdrawal of domperidone in many patients. All patients require pre-treatment with domperidone (see above) and will need to continue this treatment for many weeks after apomorphine initiation.

Postural hypotension may be experienced on initiation of apomorphine. This is transitory and should not persist.

Apomorphine may produce hypotension. Care should be exercised 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.

Apomorphine, especially at high dose, may have the potential for QT prolongation. Caution should be exercised when treating patients at risk for torsades de pointes arrhythmia.

Apomorphine has been associated with somnolence and other dopamine agonists can be associated with sudden onset of sleep. Patients must be informed of this and advised to exercise caution while driving or operating machines. Furthermore, a reduction of dosage or termination of therapy may be considered necessary.

Apomorphine therapy is associated with a moderate level of psychological and psychosexual disturbances. These effects occur particularly in patients who have previously experienced psychiatric disturbances with other dopamine agonists. Apomorphine is contraindicated in patients with pre-existing psychiatric problems.

Pathological gambling, increased libido and hypersexuality have been reported in patients treated with dopamine agonists for Parkinson's disease, including apomorphine.

Apomorphine has been implicated in a few cases of haemolytic anaemia with a positive direct Coomb's test.

Subcutaneous administration of apomorphine can cause the formation of nodules at the injection sites. These can become inflamed and, in some cases, can cause necrosis.

All adverse effects should be reported to the GP, PDNS or Consultant Neurologist for advice.

NOTABLE DRUG INTERACTIONS (REFER TO BNF AND SPC)

Patients selected for treatment with apomorphine are almost certain to be taking concomitant medications for their PD. In the initial stages of apomorphine therapy, the patient should be monitored for unusual side effects or signs of potentiation of effect.

Neuroleptic medicinal products may have an antagonistic effect if used with apomorphine. There is a potential interaction between clozapine and apomorphine, however clozapine may also be used to reduce the symptoms of neuropsychiatric complications.

If neuroleptic medicinal products have to be used in patients with PD treated by dopamine agonists, a gradual reduction in apomorphine dose may be considered when administration is by minipump and/or syringe-driver (symptoms suggestive of neuroleptic malignant syndrome have been reported rarely with abrupt withdrawal of dopaminergic therapy).

Apomorphine may cause hypotension. Care should be exercised in patients taking antihypertensives as apomorphine may potentiate the antihypertensive effects.

It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval.

BACK-UP INFORMATION/ADVICE

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REFERENCES

1. Summary of Product Characteristics for:
   a. APO-go® PFS 5 mg/ml, available at http://emc.medicines.org.uk
   b. APO-go® Pens 10 mg/ml, available at http://emc.medicines.org.uk

2. APO-go® information for both patients and healthcare professionals http://www.apo-go.co.uk/
   24/7 Telephone helpline manned by APO-go® advisers: 0844 8801327


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