INTRODUCTION

Disabling motor fluctuations are a common complication of idiopathic Parkinson’s disease. Some of these patients may 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 5-15 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.

SHARED CARE

A shared care protocol is used to facilitate the sharing of care and transfer of prescribing. This would usually take place once the patient’s condition is stable; the patient is demonstrably benefiting from the treatment and is free from any significant side effects. GPs should only take on the prescribing when they are confident in the agreed care plan advised by the specialist team. Contingency plans must be in place to enable the patient to receive the recommended treatment, should the GP decline to prescribe.

The complex nature of apomorphine administration necessitates that it should be initiated by the Movement Disorder team.

This protocol provides information on the use of apomorphine treatment for the shared care of therapy between the specialist team and the GP concerned.

SHARECARE RESPONSIBILITIES

**Aspects of care for which the Hospital Consultant is responsible**

2. Initiating treatment with apomorphine, including initial supply of the necessary equipment.
3. Organise training of patient and carers to administer apomorphine if appropriate
4. Arranging support from District Nurses if required to administer and/or prepare apomorphine for continuous infusion.
5. Liaison with GP to agree to share the patients care.
6. Gradual withdrawal of domperidone according to response (or ondansetron if domperidone was unsuitable)
7. To monitor and evaluate the response to antiparkinsonian therapy and initiate changes to therapy.
8. To monitor for and evaluate abnormal test results and any adverse drug reactions.

**Aspects of care for which the General Practitioner is responsible**

1. To inform the Hospital team of changes in the patient’s condition which may be related to treatment with apomorphine.
2. To conduct a full blood count, urea, creatinine and liver function tests, blood pressure and heart-rate measurement including direct Coombs test every 6-12 months and report results to specialist team.
3. Clinical responsibility for the prescription for apomorphine, and needles/infusion lines where required.
4. To treat local skin problems such as infection or fibrosis.

**Patient's/Carer’s/Guardian’s role**

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Report any adverse effects to the specialist or GP.
4. If wishing to self-administer, will agree to appropriate training and to protocols for the safe disposal of sharps.
INDICATION FOR THERAPY

Management of disabling motor fluctuations despite optimal oral therapy in patients with Parkinson's disease or patients who have been assessed as suitable for monotherapy with apomorphine.

PREPARATIONS AVAILABLE

Generic apomorphine 10mg/ml solution for injection
(2ml and 5ml ampoules)
- APO-go ampoules 10mg/ml solution for injection (2ml & 5ml)
- APO-go pen 10mg/ml solution for injection (3ml disposable, multiple dose, pen injector)
- APO-go PFS 5mg/ml solution for infusion (10ml pre-filled syringe)

COST (excluding VAT)

Non proprietary apomorphine 5x2ml amps each containing apomorphine 20mg £30.35

Non proprietary apomorphine 5x5ml amps each containing apomorphine 20mg £58.50

APO-GO 5 x 2 ml amps each containing apomorphine 20mg £37.95

APO-GO5 x 5ml amps each containing apomorphine 50mg £73.10

APO-GO5 x 3ml disposable pens each containing apomorphine 30mg £123.90

APO-GO5 x 10ml prefilled syringes containing apomorphine 50mg £73.10

(source: BNF 66 September 2013)

RECOMMENDED DOSAGE

The dose will be determined on an individual patient basis, typically within the range 3-30mg daily. Individual bolus injections should not exceed 10mg. The total daily dose should not exceed 100mg.

RECOMMENDED ADMINISTRATION

Premedication with oral domperidone 20mg three times a day starting 72 hours prior to initiation of therapy is essential. Baseline ECG and rationalization of medication which can prolong QT interval will be required prior to initiation due to potential issues with conduction abnormalities including QT prolongation. If it is not possible to achieve, the specialist team would consider the use of ondansetron (off label in discussion with the patient)

The route of administration will either be subcutaneous intermittent injection or continuous subcutaneous infusion, depending on patient requirements.

Intermittent subcutaneous injection:
Administered subcutaneously, to the outside of the thighs or abdomen, using a multi-dose disposable pen injector.

Subcutaneous infusion:
Administered using an APO-go PFS 5mg/ml pre-filled syringe via an APO-go pump.

The injection site should be covered using a suitable dressing eg. Tegaderm. To minimise local irritation the site of administration should be rotated daily.

APO-go pumps are available on permanent loan.

EQUIPMENT REQUIRED AND AVAILABILITY

APO-go ampoules, Apomorphine 10mg/ml ampoules, APO-GO PFS pre-filled syringes and APO-go pens and needles can be prescribed on a GP10. (Needles need to be ordered at the same time as the pens). Community pharmacists may obtain supplies direct from Genus Pharmaceuticals (tel number: 08448801327).

Transparent adhesive dressing e.g. Tegaderm 6cm x 7cm dressing can be prescribed on a GP10.

Neria lines available from Unomedical are compatible with and have been tested for use with Apomorphine.

If any issues with local reactions to Neria lines, please contact the Specialist Team to discuss

ADVERSE EFFECTS

Apomorphine is highly emetogenic. Tolerance to this effect develops in many patients allowing eventual withdrawal of domperidone. However, most patients require pre-treatment with domperidone (see above), and will need to continue on this treatment for many weeks after apomorphine initiation. If domperidone was unsuitable, the specialist team would consider the use of ondansetron (off label in discussion with the patient)

Postural hypotension may be experienced on initiating treatment. This is transitory and should not persist after discharge.

Apomorphine has been associated with somnolence, and other dopamine agonists can be associated with sudden sleep onset episodes, particularly in patients with Parkinson’s disease. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment with apomorphine. Patients who have experienced somnolence must refrain from driving or operating machines. Furthermore, a reduction of dosage or termination of therapy may be considered necessary.
Apopomorphine therapy can be associated with psychological and psychosexual disturbances. These effects occur particularly in patients who have previously experienced psychiatric disturbances with other dopamine agonists. Apomorphine is contra-indicated in patients with pre-existing psychiatric problems unless a full specialist assessment has been undertaken.

Apopomorphine has been implicated in a few cases of haemolytic anaemia with a positive direct Coombs’ test. Subcutaneous administration of apomorphine can cause necrosis, inflammation and formation of nodules at the injection site.

**CONTRAINICATIONS**

Apopomorphine is contra-indicated in patients with any respiratory depression, dementia, psychotic diseases (see above) or hepatic insufficiency. Apomorphine should not be administered to anyone with known hypersensitivity to apomorphine or any of the excipients.

**PRECAUTIONS**

Due to the age of the treated population, the occurrence of pregnancy is improbable; however, the effects of apomorphine in pregnancy are unknown, and apomorphine should be avoided in pregnant and breast-feeding mothers. Advice from tertiary specialist centre would be sought in this scenario.

**MONITORING**

Periodic clinical evaluation and monitoring of hepatic, haemopoietic including direct Coombs test, renal and cardiovascular function is advised every 6-12 months.

**DRUG INTERACTIONS**

In the initial stages of apomorphine therapy the patient should be monitored for side-effects or signs of potentiation of effect of concomitant antiparkinsonian drugs. Dose reduction of levodopa may be necessary.

Antipsychotics may antagonise the effects of apomorphine.

The possible effects of apomorphine on other drugs has not been studied; therefore caution is advised when combining apomorphine with other drugs, particularly those with a narrow therapeutic index.. Please seek advice from pharmacist.

**PHARMACEUTICAL PRECAUTIONS**

All forms of apomorphine should be stored at room temperature (no greater than 25°C) and protected from light. Solution for injection which has turned green should not be used.

APO-go pens have a 48 hour expiry once in use. PFS syringes should be discarded after 24 hours.

Contact Points
Dr Nicola Chapman, Consultant Physician Queen Margaret Hospital Tel 01383 623623 ex 23709
Dr Aylene Kelman 28441 (or supervising Consultant)
Joy Reid/Nancy Gallagher, Parkinson’s Nurse Specialists Ward 12 VHK, Tel 01592 643355 ext 28834
Monica Davies, Senior Pharmacist 01592 643355 ext 28449

Useful references
Apomorphine - summary of product characteristics
UCL Apomorphine Shared Care Guidelines 5th Edition 2005
www.emc.medicines.org.uk
www.Apo-go.co.uk

Any queries regarding the Shared Care Protocol - contact the Clinical Effectiveness Pharmacist. Tel no. (01592) 226915
Document Approved on behalf of NHS Fife by NHS Fife Area Drugs and Therapeutics Committee
Ishliaq Mohammed Clinical Effectiveness Pharmacist.