NHS
Pan Mersey
Area Prescribing Committee

Prescribing Support Information

APOMORPHINE injection

AMBER patient retained by specialist

Apomorphine is classed as Amber Patient Retained by the Pan Mersey Area Prescribing Committee.

Apomorphine has been considered to be appropriate for prescribing in primary care and the information contained in this document has been provided to support GPs to prescribe apomorphine for their patients after specialist initiation.

Patients on apomorphine will remain under the care of the specialist team and be regularly monitored whilst receiving this medication.

Who will diagnose and decide who is suitable for apomorphine?

Neurology specialists or a geriatrician with a special interest in Parkinson's disease will assess and select patients with Parkinson's disease who are suitable for apomorphine therapy. This decision will be communicated to the GP along with a patient care agreement letter to request GP agreement to prescribe ongoing supplies of apomorphine after patient has commenced therapy. This is to avoid subsequent difficulty with continuation of treatment for the patient after initial supplies from the specialist have been used.

Licensed indication and mode of action

Apomorphine is licensed for the treatment of refractory motor fluctuations in Parkinson's disease ('off' episodes) inadequately controlled by co-beneldopa or co-careldopa or other dopaminergics[1].

Apomorphine is a direct dopamine agonist with no opiate or addictive properties. The rapid onset of action is an advantage when patients are experiencing frequent or severe "off" periods. It can be administered at the onset of an "off" period and has a rapid onset of effect (4-12 minutes) and duration of action of about 1 hour. Where overall control remains unsatisfactory, or for patients who require frequent injections, continuous subcutaneous infusion is considered.

Dosage and administration

Apomorphine is given by subcutaneous route **only**, via intermittent injection or continuous infusion. It must always be prescribed by brand to avoid confusion and to ensure the patient always receives the same product.

<u>Available Preparations:</u>

Pre-filled Pen 30mg/3ml - for intermittent injection, pen to be discarded no later than 48 hours from first use.

Pre-filled Syringe 50mg/10ml - for immediate single use for infusion, remainder of solution should be discarded.

Optimum dose will be established by the specialist and varies widely between individual patients.

By subcutaneous injection, adult over 18 years:

Usual range 3–30 mg daily in divided doses, subcutaneous infusion may be preferable in those requiring division of injections into more than 4-6 doses daily; maximum single dose is 10 mg. Maximum licensed dose 100mg daily.

By continuous subcutaneous infusion, adult over 18 years:

Standard rate 1-4 mg/hour (15-60 micrograms/kg/hour), some patients may require 8-10mg/hour. Intermittent boluses via the pump maybe needed. The infusion site should be changed every 12 hours.

The total licensed daily dose of apomorphine is 100mg. Higher doses are occasionally prescribed and informed consent will be gained from the patient by the specialist when using doses above the licensed maximum. This will be communicated to the GP.

The hours of use of the apomorphine pump will be determined on an individual patient basis by the specialist team.

The dose, infusion rate and hours of use may only be altered by the specialist.

Cautions and contraindications

Contraindications will be assessed by the specialist team. Please refer to the Summary of Product Characteristics (SPC) for the complete list.

Side effects

- Local indurations and nodule formation at injection site, particularly with continuous use.
- Nausea and vomiting – prevented by treatment with domperidone, see below.
- Transient sedation and yawning.
- Confusion and postural hypotension.
- Somnolence.
- Neuropsychiatric disturbances.
- Development of impulse control disorders.
- Autoimmune haemolytic anaemia.

Please note this list is not exhaustive – refer to SPC for the complete list.

Domperidone to prevent nausea and vomiting

To avoid nausea and vomiting, domperidone 10mg three times daily should be started 48 hours prior to first treatment with apomorphine. Thereafter the dose is 10mg three times daily for as short a time as possible – which will be determined by the specialist team.

MHRA guidance on use of domperidone has an exception for PD patients who may need domperidone for longer periods or at higher doses[2].

If nausea is severe despite 10mg three times daily, the dose may be increased to 20mg three times daily but only after careful consideration and an ECG shows no QTc interval prolongation. Subsequently domperidone dose will be reviewed with the aim to reduce and possibly stop. However, some patients may require ongoing treatment with domperidone, preferably at 10mg three times daily and discontinuation of apomorphine is not considered possible by the specialist team and the patient has made an informed decision.

The GP may be contacted to prescribe the domperidone prior to the patients' first treatment and to prescribe ongoing treatment if deemed necessary.

ECG Investigation

Both apomorphine and domperidone may prolong QTc interval and although the cardiac risk is very small, an ECG to check the QTc interval (normal <0.44sec) is required prior to use of apomorphine or domperidone. The hospital will arrange this.

Patients with prolonged QTc on ECG or taking other drugs known to cause QT prolongation (such as ketoconazole / erythromycin / some SSRIs) should not start domperidone or apomorphine without careful re-evaluation of the risks and benefits by the specialist.

An ECG is required during the first month of therapy and the hospital / specialist nurse will arrange this.

An ECG should be repeated to check QTc if there are symptoms of arrhythmia (syncope / loss of consciousness / palpitation) or if other QT prolonging drugs are added to the patient's prescription.

Drug interactions

Neuroleptics and methyldopa may antagonise the effect of apomorphine. Memantine may enhance effect of apomorphine. Apomorphine may potentiate the hypotensive effects of other drugs; use with caution in patients with pre-existing cardiac disease or postural hypotension.

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

Please refer to SPC for full list of drug interactions.

Monitoring

No specific biochemical monitoring is required by the GP. Direct Coombs test will be monitored by specialist team.

Who will increase the dose?

The specialist team will decide on the ongoing dose, frequency, duration of therapy and subsequent dosage adjustments of apomorphine, domperidone and other anti-Parkinson's medication and will inform the patient and their GP of any changes.

Who is responsible for stopping the drug?

Apomorphine should only be stopped by the specialist team.

When to seek specialist advice/review

Consider seeking specialist advice if any adverse effects are reported by the patient. Any deterioration in symptoms should be reported e.g. decline in motor performance, hallucinations, confusional states, psychosis, depression or an inability to administer apomorphine. Development of impulse control disorders will be monitored by the specialist team, but if this is noted in the community please seek specialist advice urgently.

When will the patient be discharged?

The patient will remain under the care of the referring Trust for the duration of the apomorphine treatment and NOT discharged to primary care.

Who will follow up the patients?

The specialist team will continue to review and follow up the patient for the duration of the apomorphine therapy.

Responsibilities of the specialist recommending apomorphine therapy:

1) Select patients requiring apomorphine therapy with due consideration of the contra-indications and precautions in the product Summary of Product Characteristics (SPC).

2) Before commencing apomorphine, send a copy of the patient care agreement letter and obtain GP agreement to prescribe ongoing supplies of apomorphine and domperidone after patient has commenced therapy.

3) Provide an explanation to the patient and request their informed consent to apomorphine treatment and document this in the patient hospital notes.

4) Initiate and monitor apomorphine treatment, until the patient is established on treatment. Prescribe and supply apomorphine for the first month of treatment.

5) Decide on the ongoing dose, frequency, duration of therapy and subsequent dosage adjustments of apomorphine, domperidone and other anti-Parkinson's medication, liaise with relevant specialist nurse about this and inform the patient and their GP.

6) Assess the patient regularly as necessary for the duration of apomorphine therapy and perform and monitor Direct Coombs test. FBC and Coombs test will be checked before initiation of treatment.

7) Ensure the patient understands the nature and complications of apomorphine therapy and their role in reporting adverse effects promptly.

8) Arrange (with specialist nurse) the ordering and supply of dedicated apomorphine pump if required for continuous infusion via pharmaceutical supplier.

9) Arrange training of the patient or carer on how to prepare and administer apomorphine.

10) If required arrange for district nursing services to prepare/administer injections/infusion.

11) Write to the GP after initiation of apomorphine, including the following information:

    - relevant clinical details
    - details of any monitoring to be undertaken by GP, dose and frequency of apomorphine and any other treatment or drugs that the patient is to receive
    - date of next outpatient appointment

12) Ensure the GP is kept informed of any changes in the patients' treatment or clinical circumstances.

13) Review the patient promptly if required by the GP concerned.

GP responsibilities:

1) Reply to consultant patient care agreement request within 10 working days.

2) Prescribe apomorphine at the dose advised by the specialist/specialist nurse.

3) Dressings will be supplied by the District Nurse team to cover the injection site for patients on continuous subcutaneous infusion if required and indicated by the specialist.

4) Monitor patients' general wellbeing.

5) Report any adverse events of treatment to the specialist, or deterioration in symptoms e.g. motor performance, hallucinations, confusional states, psychosis, depression or an inability to administer apomorphine.

6) Prescribe domperidone treatment until advised to stop by specialist.

7) Inform the specialist of any relevant change in the patients' circumstances.

8) Prescribe infusion lines as per details in the clinic letter from the specialist. Neria infusion lines are the recommended lines to be used for subcutaneous infusion. The specific lines to be used will be communicated via clinic letter as these can vary, particularly for frail patients.

   In the event there is a supply problem with infusion lines please contact the Parkinson's Disease specialist nurse at the Trust for advice.

References

1. Summary of Product Characteristics for apomorphine. SPC
2. MHRA Drug Safety Update 11 December 2014. Domperidone: risks of cardiac side effects. Domperidone