Shared Care Guideline: *Apomorphine*

County Durham and Darlington Area Prescribing Committee

Drug	Apomorphine
Indication	Advanced Parkinson's Disease in adults (18 years and over)
Overview	Apomorphine is a dopamine agonist licensed for use in patients with advanced Parkinson's disease who have frequent and/or severe akinesia ("off periods") not controlled by levodopa or other dopaminergic treatments. It is given as a continuous subcutaneous infusion, usually over 12 hours, or as an intermittent injection, at the onset of an "off-period"..
Specialist's Responsibilities	**Initial investigations:** Full Blood Count (FBC), reticulocyte count and Coombes test(haemolytic anaemia) An ECG should be performed and QT interval assessed prior to treatment with domperidone, during the treatment initiation phase and as clinically indicated thereafter **Initial regimen:** Domperidone pre-loading to reduce nausea and vomiting. Threshold dose and effective dose determined during a period of in-patient monitoring. Patient and carer education prior to discharge. Dose calculated for individual patient dependant on Apomorphine challenge, and will be confirmed for each patient in the Clinic Letter. Doses would not *normally* exceed 4mg/hour. **Clinical monitoring:** For effectiveness and adverse effects. FBC, reticulocyte count and Coombes test. Reduction of domperidone after 2-3 months. On-going adjustment of apomorphine dose. **Frequency:** Initially as inpatient, typically 1 to 3 monthly until stabilised, either as outpatient or home visit monitoring. **Safety monitoring:** • Monitoring for response and adverse drug reactions (ADRs) during the initiation period. • Evaluating ADRs raised by the GP and evaluating any concerns arising from physical checks and reviews undertaken by GP

	Prescribing duration: Specialist to prescribe medication until patient is on stable dose, then shared care is requested. Specialist to continue to prescribe until shared care is accepted by GP **Communication and Documentation to GP:** • Obtaining agreement of GP to participate in shared-care arrangement for apomorphine therapy (by sending a copy of this document and letter to the GP). • Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment. • Provide additional information and advice to the GP on actions he/she may need to take e.g. on dosage adjustment, other changes in therapy and management of adverse effects, as required. • Clinic letters and results to GP.
GP's Responsibilities	**Maintenance prescription:** Prescribe apormorphine in accordance with the specialist's recommendations as outlined in the shared care agreement. Sub-cutaneous (SC) infusion: 1 to 4mg per hour, doses will not normally exceed 100mg/per day. Intermittent SC injection: individualised dose as at transfer of care. **Clinical monitoring:** FBC, reticulocyte count and Coombes test. **Frequency:** SIX monthly **Safety Monitoring:** • Monitoring for response and adverse drug reactions (ADRs) during the initiation period. • Evaluating ADRs raised by the GP and evaluating any concerns arising from physical checks and reviews undertaken by GP **Criteria Requiring Specialist contact::** • Failure to attend for review • Intolerance of drugs • Communications failure **Documentation to specialist:** • Reply to request for shared-care as soon as practical (within 28 days) • Blood results to specialist via use of patient-held record.

Adverse Events

Adverse event	Action to be taken
Nausea , vomiting	Domperidone 20 to 30 mg, 2 or 3 times per day
Significant clinical deterioration(motor, confusion, hallucinations, psychosis)	Contact consultant or movement disorder nurse specialist
Significant skin irritation/nodules	Contact movement disorder nurse specialist
Abnormal FBC. May include haemolytic anaemia, thrombocytopaenia and eosinophilia.	Contact consultant or movement disorder nurse specialist

Other adverse effects include the following (note list is not exhaustive – see current edition of BNF and SPC.)

- Drowsiness,
- sudden onset of sleep,
- Yawning
- Dyspnoea
- Postural hypotension
- Rash
- Impulse control disorders: (pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur)

Contra-indications	**Contraindications** • Known hypersensitivity to apomorphine • Pregnancy • Breast feeding. • Absence of someone to deliver SC injection • Hepatic impairment • Neuropsychiatric problems • Dementia • Respiratory depression • Hepatic insufficiency
Cautions	• history of postural hypotension (special care on initiation) • pulmonary disease • susceptibility to QT-interval prolongation • Particulary when used in combination with domperidone: serious underlying heart conditions, significant electrolyte disturbance (and medication possibly affecting electrolyte balance), hepatic impairment. • Sulphite allergy (avoid if severe) • Avoid if 'on' response to levodopa marred by severe dyskinesia or dystonia
Drug Interactions	• effects of apomorphine antagonised by antipsychotics • effects of apomorphine possibly enhanced by entacapone • possible increased hypotensive effect when apomorphine given with ondansetron—avoid concomitant use • Apomorphine may potentiate the antihypertensive effects of antihypertensive and other cardioactive medicinal products. • possible increased risk of ventricular arrhythmias when apomorphine given with domperidone. It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval (see below) • <u>QTc-prolonging medicinal products</u> - anti-arrhythmics class IA (e.g., disopyramide, hydroquinidine, quinidine) - anti-arrhythmics class III (e.g., amiodarone, dofetilide, dronedarone, ibutilide, sotalol) - certain antipsychotics (e.g., haloperidol, pimozide, sertindole) - certain antidepressants (e.g., citalopram, escitalopram) - certain antibiotics (e.g. , erythromycin, levofloxacin, moxifloxacin, spiramycin) - certain antifungal agents (e.g., pentamidine) - certain antimalarial agents (in particular halofantrine, lumefantrine) - certain gastro-intestinal medicines (e.g., cisapride, dolasetron, prucalopride) - certain antihistaminics (e.g., mequitazine, mizolastine)

	- certain medicines used in cancer (e.g., toremifene, vandetanib, vincamine) - certain other medicines (e.g., bepridil, diphemanil, methadone) (see section 4.3). • Potent CYP3A4 inhibitors (regardless of their QT prolonging effects) - protease inhibitors - systemic azole antifungals - some macrolides (erythromycin, clarithromycin and telithromycin) ***Please refer to SPC or BNF for full details of adverse effects, contraindications, cautions and drug interactions.***
Other Information	It is usually possible to withdraw domperidone after 2 to 3 months (this will be managed by the hospital team). Other anti-parkinsonian medication maybe reduced or withdrawn by the specialist team. Movement disorder Nurse Specialist is available if concerns arise. Once mixed for use apomorphine is only stable for 48 hours.
Contact Details	Thank you for sharing the care of this patient. If you have any concerns or queries, please contact the Consultant or secretary. Patients are provided with contact details of Movement disorder team and contact for Genus Pharma helpline (0844 880 1327). All clinic letters will be copied to patient. Parkinson Disease Specialist Nurses, Darlington Memorial Hospital, Hollyhurst Road, Darlington, County Durham DL3 6HX Tel: 01325 743000