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GMMMG Interface Prescribing Subgroup

Shared Care Template

GMMMG NHS

Shared Care Guideline for Apomorphine use in Parkinson's Disease		**Reference Number**
Version: 3	**Replaces: Version 2**	**Issue date: 01/02/2016**
Author(s)/Originator(s): (please state author name and department) *Carol Miller, Emma Wilson and Chris Kobylecki* *Salford Royal Hospital* *Neurology Department*		**To be read in conjunction with the following documents:** Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Interface Prescribing Group: *dd/mm/yyyy*		**Date approved by Greater Manchester Medicines Management Group:** *dd/mm/yyyy*
Date approved by Commissioners: *dd/mm/yyyy*		**Review Date:** *01/01/2018*

Please complete all sections

1. Name of Drug, Brand Name, Form and Strength	Apomorphine (APO-go®) 10mg/ml Solution for Injection in 3ml PEN or 5mg/ml Solution for Infusion in Pre-Filled Syringe in 10ml syringe (PFS)
2. Licensed Indications	The 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
3. Therapeutic use & background	Parkinson's disease is a progressive degenerative neurological condition that affects nerve cells in the substantia nigra and basal ganglia (the parts of the brain controlling movement). Parkinson's disease is caused by idiopathic degeneration of dopamine producing cells in this area. Three 'cardinal signs' of Parkinson's disease are resting tremor, cogwheel rigidity and bradykinesia. Postural instability, typically a late finding in Parkinson's disease is the fourth main symptom. Parkinson's disease is characterised by a good symptomatic response to levodopa. Parkinson's disease is one of the commonest neurological conditions to affect older people. It is estimated to affect 160 per 100,000 of the general population. Apomorphine is licensed for the 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. Apomorphine treatment is to be initiated, and doses optimised by the hospital specialist team. Continuation of the therapy requires co-operation between the hospital and CCG teams with their roles defined by the shared care protocol. Apomorphine is a directly acting dopaminergic agonist, licensed for use in patients with Parkinson's disease who have frequent and/or severe akinesia ("off periods") not controlled by levodopa or other dopamine agonists Apomorphine is a dopamine agonist, which acts directly on D_1 and D_2 receptors, stimulating areas of the brain where dopamine works. It produces a similar effect to levodopa, that is, the ability to prevent and reverse disabling "off" periods. Despite its name it has no opiate or addictive properties. Apomorphine cannot be used orally because it undergoes extensive first pass metabolism (in the liver) to an inactive metabolite; for this reason it is administered subcutaneously. • Apomorphine may be administered as a "rescue therapy" with intermittent subcutaneous bolus injections given via a prefilled Apomorphine Pen: 10mg/ml Solution for Injection in a 3ml Pen (Apomorphine Pen) Patients selected for treatment with Apomorphine should be able to recognise the onset of their 'off' symptoms and be capable of injecting themselves or else have a responsible carer able to inject for them when required • For those patients who experience more complex motor fluctuations, including dyskinesias, a continuous subcutaneous infusion using an ambulatory Apomorphine pump may be used with the Apomorphine PFS: 5mg/ml Solution for Infusion in Pre-Filled Syringe in a 10ml syringe (Apomorphine PFS) • Apomorphine Ampoules 10mg/ml is also available in 5ml ampoules for continuous infusion
4. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	• Children and adolescents (up to 18 years of age) • Known sensitivity to Apomorphine or any other ingredients of the product. • Respiratory depression • Dementia • Psychotic disease • Hepatic insufficiency • Intermittent Apomorphine HCl treatment is not suitable for patients who have an 'on' response to levodopa which is marred by severe dyskinesia or dystonia *With Caution:* • Pulmonary, renal or cardiovascular disease • Persons prone to nausea and vomiting • Elderly and/ or debilitated patients • Pre-existing cardiac disease or in patients taking vasoactive medicinal products such as antihypertensives, and especially in patients with pre-existing postural hypotension • Ondansetron should be used with caution due to the risk of hypotension
5. Prescribing in pregnancy and lactation	*This shared care protocol does not cover pregnant or breastfeeding women. Under these circumstances prescribing will remain the responsibility of Specialist.*
6. Dosage regimen for continuing care	Route of administration: *Subcutaneously* Preparations available: • 5mg/ml Solution for Infusion in Pre-Filled Syringe 10ml syringe (Apomorphine PFS) • 10mg/ml Solution for Injection in a 3ml Pen (Apomorphine Pen) • Apomorphine Ampoules 10mg/ml is also available in 5ml ampoules for continuous

infusion

- The optimal dosage of Apomorphine has to be determined on an individual patient basis and the threshold dose is determined by the specialist using incremental dosing schedules. Once the optimal dose for an individual patient has been determined and the patient is stable, the dose is likely to remain relatively constant
- The daily dose of Apomorphine varies widely between patients,
- Intermittent injection – typically 1-10 injections per day, each dose no more than 10mg
- Continuous infusion - typically 1–6 mg per hour (but may be higher, dependent upon individual response), mostly during waking hours but may be necessary for overnight infusion according to patient's needs. Considered if the patient experiences so many 'off' periods that repeated bolus injections are inappropriate.
- Maximum licensed daily dose by either route is 100 mg. Any doses prescribed over 100mg are with documented Consultant consent and the GP will be informed. This makes the dose unlicensed and the GP may no longer wish to be involved in shared care.
- Apomorphine is occasionally used for patients with swallowing difficulties and at the palliative stage

Is titration required	Yes but not by GP	

- Titrate dosage up by 0.5mg-1mg increments hourly; however the time may vary depending on whether a patient is an inpatient or in the community. Judgement of specialist Consultant or PDNS.
- Maximum licensed daily dose by either route is 100 mg. Any doses prescribed over 100mg are with documented Consultant consent and the GP will be informed. This makes the dose unlicensed and the GP may no longer wish to be involved in shared care.

Adjunctive treatment regime:

As per the Association of British Neurologists (ABN) guidance it is essential that the patient is established on Domperidone 20mg oral TDS daily, 48 hours prior to initiation of Apomorphine. The dose should be reduced to 10mg tds after 2 weeks if the patient is not experiencing nausea.

If the prescribed dose is maintained at more than 30 mg daily then the ECG should be repeated after 2 weeks.

Reduction or withdrawal should be regularly considered.

There is a **low risk** of prolonged QT interval which could lead to ventricular arrhythmia. Patients should not be given domperidone whilst on medications known to prolong the QT interval or strongly inhibit CYP3A4 eg, ketoconazole or erythromycin.

Please see the Association of British neurologists (ABN) guidance for domperidone

https://gallery.mailchimp.com/7f92fc52090d776e2c33ff870/files/domperidone.pdf

	Conditions requiring dose reduction (to be determined by treating specialist team): e.g. impaired renal/ liver function • Hypotension which is symptomatic to patient. • Cognitive impairment • Hallucinations • Obsessive compulsive disorder • Impulse control disorder
	Usual response time: Following a single dose, Apomorphine has an onset of action of 4-12 minutes and lasts for about one hour with the Apomorphine Pen or is continuous with the infusion with the Apomorphine PFS.
	Duration of treatment: Apomorphine therapy is a treatment for a chronic disease and therefore course length can be many years. It is used in complex Parkinson"s disease and when the disease is beginning to fluctuate, but is not controlled with oral medication.
	Treatment to be terminated by: Specialist Consultant or Parkinson"s Disease Nurse Specialist
	NB. All dose adjustments will be the responsibility of the initiating specialist.
7.Drug Interactions ***For a comprehensive list consult the BNF or Summary of Product Characteristics***	The following drugs must <u>not</u> be prescribed without consultation with the specialist: It is recommended to avoid the administration of Apomorphine with other drugs known to prolong the QT interval. Examples being: Amiodarone, Chlorpromazine, Cisapride, Citalopram, Clarithromycin, Clomipramine, Disopyramide, Erythromycin, Flecainide, Haloperidol, Mesoridazine, Moxifloxacin, Pentamidine, Procainamide, Sotalol, Vandetanib See BNF for full details
8. Adverse drug reactions *For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of*	Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Adverse event System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**
Localised discomfort at needle site	Assessment	Nurse

Product Characteristics or BNF	Nodule formation at needle or infusion site. Usually asymptomatic but may persist in patients on high doses. Severe nodule formation may lead to worsening of symptoms due to erratic absorption of Apomorphine	Rotate injection site. Massage to injection sites is recognised to reduce nodule formation. Ultrasound therapy has been anecdotally said to alleviate severe nodule formation. Anecdotally Hirudoid cream can be used on nodules	Patient / carer
	Nausea & vomiting. Usually transient and resolved within 6-8 weeks	Treatment with Domperidone 20mg oral TDS daily, 48 hours before and during Apomorphine therapy is essential .The dose should be reduced to 10mg TDS after 2 weeks. Once treatment has been established Domperidone* therapy may be gradually reduced and can be successfully discontinued in most patients within 6-8 weeks * please refer to latest recommendations for Domperidone Where Domperidone is contraindicated, consider requesting secondary care to prescribe Ondansetron	GP as advised by Consultant / PDNS
	Allergic reactions including bronchospasm and anaphylaxis (due to sodium bisulphate)	Withhold and discuss with Consultant/PDNS	GP
	Light-headedness	Discuss with Consultant /PDNS	GP
	Postural hypotension is seen infrequently and is usually transient	Care should be exercised in patients with pre-existing cardiac disease or in patients taking vasoactive medicinal products such as antihypertensives, and in patients with pre-existing postural hypotension.	GP
	Dyskinesias during 'On' periods	Discuss with Consultant /PDNS	GP

	Coombs positive Haemolytic anaemia	Coombs' test is carried out at baseline. If positive, the patient should have a further blood screen of the same parameters after one month's treatment and then have FBC and reticulocyte count at 6 monthly hospital visits from then on but no requirement to keep doing Coombs' tests provided FBC remains normal	Consultant/PDNS as required
	Eosinophilia in up to 10% of patients	Discuss with Consultant /PDNS	GP
	Dopamine dysregulation, neuropsychiatric complications – hallucinations, euphoria, increased libido, confusion, personality changes, agitation, restlessness, psychosis, sleep disturbances, pathological gambling and over eating	Discuss with Consultant /PDNS	GP
	Sedation. Usually transient	Advise patients not to drive / operate machinery if affected. If persists discuss with Consultant / PDNS	GP
	The patient should be advised to report any of the following signs or symptoms to their GP without delay: N/A		
	Other important co morbidities (e.g. Chickenpox exposure). Include advice on management and prevention and who will be responsible for this in each case: N/A		
	Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.		
9.Baseline investigations	*List of investigations / monitoring undertaken by secondary care* Baseline assessment should include lying and standing blood pressure, FBC, reticulocyte count and a Coombs' test, which will be carried out by secondary care. No requirement for ECGs on patients unless there is a history of cardiac dysrhythmia or severe ischaemic heart disease, if required secondary care will arrange. During hospital visits the patient should have a further blood screen of the same parameters after one month's treatment and then have FBC and reticulocyte count at 6		

	months and 12 months. If the results are within normal parameters at this stage then they should be repeated annually but no requirement to keep doing Coombs tests.				
10. Ongoing monitoring requirements to be undertaken by GP	**Is monitoring required?**	**Yes or No (if yes complete following section)**			
	Monitoring	**Frequency**	**Results**	**Action**	**By whom**
	FBC	6 monthly	Communicated to Consultant/PDNS	Communicated to Consultant/PDNS	GP/Secondary care
11. Pharmaceutical aspects	*e.g. special storage requirements, washout periods Or where there are "no special considerations"* Do not store above 25°C. Store in the original package. Do not use if the solution has turned green. The solution should be inspected visually prior to use. Only clear, colourless solutions should be used.				
12. Criteria for shared care	Prescribing responsibility will only be transferred when • Treatment is for a specified indication and duration. • Treatment has been initiated and established by the secondary care specialist. • The patient's initial reaction to and progress on the drug is satisfactory. • The GP has agreed in writing in each individual case that shared care is appropriate. The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements				
13. Patients excluded from shared care	Unstable disease state N/A				
14. Responsibilities of initiating specialist	• Patient suitability/selection • Provision of information to patient & primary care team regarding Apomorphine therapy. • Baseline tests as described above • Provision of information to patient, carer (DVD and written material) • To arrange prescription for /prescribe Domperidone* 20mg oral TDS daily, 48 hours prior to initiation/response test of Apomorphine • Arrange Apomorphine challenge/initiation within outpatient clinic, community setting or hospital inpatient clinic • Arrange provision of patient/carer education and training • Provision of information to primary care team • Arrange infusion pump training for District Nurses • Advise District Nurse as required on dose and titration • Agree with GP responsibility for 6 monthly FBC if required • Optimisation and evaluation of medication • Monitor and evaluate potential adverse drug reactions • Provision of information and support to patient, carers and primary care team as appropriate • Provide point of contact for community team and patients • Monitor blood results • Provide clear, documented advice about changes if necessary				

15. Responsibilities of the GP & District Nurses	GPs: • Reply to request for shared care within 14 days • Prescribe ongoing Apomorphine and any concomitant therapy i.e. Domperidone (FP10s). • Report side effects or issues relating to Apomorphine treatment to PDNS/treating Consultant • 6 monthly FBCs as advised specialist team • Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary • To monitor and prescribe in collaboration with the specialist according to this protocol • Provision of dressings, lines and sharps bins District Nurses: • Supervision and support as required • Inform PDNS/GP/treating Consultant of any problems • Report side effects or issues relating to Apomorphine treatment to PDNS/treating Consultant and GP • Maintain appropriate level of knowledge and skills.			
16. Responsibilities of the patient	• To take medication as directed by the prescriber, or to contact the GP if not taking medication • Collects prescription as per practices repeat prescription procedure for dispensing at community pharmacy • Attend Outpatient and GP appointments • Attend appointments for tests • Report concerns and adverse events to GPs / PDNS / Specialist NB: Ongoing prescribing may depend on attendance at clinics as requested by the clinicians			
17.Additional Responsibilities e.g. Failure of patient to attend for monitoring, Intolerance of drugs, Monitoring parameters outside acceptable range, Treatment failure, Communication failure	**List any special considerations**	**Action required**	**By whom**	**Date**
	N/A	N/A	N/A	N/A
18. Supporting documentation	The Summary of Product Characteristics (SPC) must be accompanied by a patient information leaflet.			
19. Patient monitoring booklet	N/A			
20. Shared care agreement form	Attached below			
21. Contact details	See Appendix 1			

Appendix 1 – Local Contact Details

Lead author contact information	**Name:** Carol Miller
	Email: carol.miller@srft.nhs.uk
	Contact number: 0161 206 1887
	Organisation: Salford Royal Hospital

Commissioner contact information	**Name:** *[insert text here]*_____
	Email: *[insert text here]*_____
	Contact number: *[insert text here]*_____
	Organisation: *[insert text here]*_____

Secondary care contact information	**If stopping medication or needing advice please contact:**
	Dr *[insert text here]*_____
	Contact number: *[insert text here]*_____
	Hospital: *[insert text here]*_____

Shared Care Agreement Form

Specialist request

***IMPORTANT: ACTION NEEDED**

Dear Dr *[insert Doctors name here]*

Patient name: *[insert Patients name here]*
Date of birth: *[insert date of birth]*
Diagnosis: *[insert diagnosis here]*

This patient is suitable for treatment with *[insert drug name]* for the treatment of *[insert indication]*

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by Trust / CCG / GMMMG). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on *[insert date started]* *[insert dose].*

If you are in agreement, please undertake monitoring and treatment from *[insert date]*
NB: date must be at least 1 month from initiation of treatment.

Baseline tests: *[insert information]*

Next review with this department: *[insert date]*
You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice. The patient will not be discharged from out-patient follow-up while taking *[insert text here]*.

Please use the reply slip overleaf and return it as soon as possible.

Thank you.

Yours

[insert Specialist name]

Shared Care Agreement Form

GP Response

Dear Dr *[insert Doctors name]*

Patient *[insert Patients name]*

Identifier *[insert patient date of birth/address]*

I have received your request for shared care of this patient who has been advised to start *[insert text here]*

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

My reasons for not accepting are: *(Please complete this secton)*

GP signature Date

GP address/practice stamp