SHARED CARE PRESCRIBING GUIDELINE APO-go® (Apomorphine) for the treatment of Parkinson's in ADULTS

APO-go® (Apomorphine) for the treatment of Parkinson's in Adults NOTES to the GP

The information in the shared care guideline has been developed in consultation with CCGs in South East London and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing APO-go® (Apomorphine) for the treatment of **Parkinson's**

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local CCG Medicines Management Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email to the requesting clinician if you are in agreement to participate in shared care.

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of APO-go® (Apomorphine) for Parkinson's can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

AGREEMENT TO PARTICIPATE IN SHARED CARE
APO-go® (Apomorphine) for treatment of Parkinson's

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient Agreement:**
Hospital requesting shared care:	Patient agrees to shared care £ Patient does not agree to shared care £

The above patient has been started on
APO-go® (Apomorphine) hydrochloride 10mg/ml pens £
OR
APO-go® (Apomorphine) hydrochloride 5mg/ml prefilled syringes £
OR
BOTH £
(Please see section 3. Place in therapy, with reference to product choice as well as individual clinic letter)

GP Name:

This is to confirm that I agree to participate in shared care for APO-go® (Apomorphine) for the treatment of Parkinson's for this patient as outlined in this shared care document

GP Signature:

Date signed:

ACTION

1. HOSPITAL CONSULTANT

Tick to confirm

§ Explain shared care to patient and obtain agreement Date agreement obtained:_____ o
§ Indicate requesting hospital o
§ Complete and sign agreement o
§ Email full shared care guideline (including signed agreement to GP) o
§ Place original in patient's notes o

2. GP PRACTICE

§ If **in agreement** to participate in shared care, sign and email (via secure NHS.net) this sheet back **within 2 weeks** of receipt **of request from specialist** to either:

§ If **do not agree** to participate in shared care, contact consultant and local Primary Care CCG Medicines Management Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local Primary Care CCG Medicines Management team should be informed.
§ Once decision reached file a copy in the Patient's medical notes.

APO-go® (Apomorphine) Hydrochloride 10mg/ml Pens and APO-go® (Apomorphine) Hydrochloride 5mg/ml Pre-filled Syringes

APO-go® (Apomorphine) is a parenteral dopamine agonist. It is used for the treatment of motor fluctuations ("on-off" phenomena) in patients with Parkinson's which are not sufficiently controlled by oral anti-Parkinson medication.

CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with **two weeks** supply of therapy

2. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Establish or confirm diagnosis and assess patient suitability for treatment
- Baseline monitoring:
- ECG (for patient convenience) GP may be requested to carry out ECG and send results to KCH), Apomorphine challenge, baseline bloods and assessments including measuring UPDRS (Unified Parkinson's Disease Rating Scale) part 3 to assess motor function, baseline lying and standing blood pressure and timed walk if possible.
- In addition to assessment of effect of treatment on quality of life and non-motor assessments, a repeat UPDRS part 3 will be performed on each visit to monitor motor progression of Parkinson's
- Discuss treatment with the patient and ensure they have a clear understanding of it. Where appropriate obtain signed consent.
- Provides the patient with information and advice, supported by written and audio information if required, explaining the treatment and use of equipment.
- Email a signed shared care guideline with patient details completed to GP for consideration of shared care request.
- Contact GP directly if response to shared care request has not been received within two weeks
- Initiate treatment and provide a minimum of two weeks supply to the patient.
- Send a copy of the clinical management plan to the GP
- Provides training and support and advice to GPs, community pharmacist, district nurses, the patient, family and carers.
- Ensuring patient fits criteria for use of this drug (e.g. no contraindications, cautions, fits local agreement for use of the drug)
- To review patient as soon as possible at the request of GP should any problems arise (side-effects / lack of efficacy).
- To communicate promptly (within 2 weeks) with the GP if treatment is changed
- To report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk

General Practitioner responsibilities

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the agreement on page 3
- If do not agree to shared care discuss with requesting consultant or local primary care medicines management team within 2 weeks of receipt of shared care request
- To provide ongoing prescriptions for APO-go® (apomorphine) and associated items to allow home administration including neria lines and sharps bin after 2 weeks.
- To agree monitoring requirements with specialist – see page 5 of this document for GP monitoring requirements.
- To report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team
- To advise the specialist if non-compliance is suspected
- To refer back to specialist if the patient's condition deteriorates.
- To stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- To report any suspected adverse effects to the MHRA via the Yellow Card scheme:: http://www.yellowcard.gov.uk

Patient's / Carer's responsibilities

- To contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs.
- To inform community pharmacists that they are using apomorphine before purchasing medication over-the-counter.
- To attend all hospital and GP appointments
- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others.

Patient's / Carer's responsibilities (continued)

§ To read the patient information leaflet included with the medication.
§ To report any adverse effects or warning symptoms to GP or hospital specialist
§ To inform GP and hospital of any changes in addresses or telephone contact numbers.

3. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for APO-go® (**Apomorphine)** prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Indication(s)

Treatment of motor fluctuations ("on-off" phenomena) in patients with Parkinson's which are not sufficiently controlled by oral anti-Parkinson medication.

Place in Therapy

Apomorphine is indicated in patients with Parkinson's who display one or more of the following symptoms; predictable or unpredictable "on-off" motor fluctuations, disabling biphasic or peak dose dyskinesia (unresponsive to therapies such as levodopa, dopamine agonists and enzyme inhibitors), and dystonia not controlled with oral therapy. See also NICE guidance for further information.

For example:

The intermittent injections (pre-filled pens) are used where patients have unpredictable 'off' (sometimes described as freezing episodes) and need 'rescue' therapy to get going quickly.

The infusion (pre-filled syringes used to fill a Chrono pump) are used where patients have motor complications affecting their current therapy regime for example considerable off time, or requiring rescue doses of apomorphine too frequently or suffering troublesome dyskinesias which are preventing titration of therapy.

Dose & route of administration

Apo-go® (Apomorphine) is available as either an intermittent subcutaneous injection, via a pre-filled pen, or by continuous subcutaneous infusion (using pre-filled syringes), during waking hours (or in some individuals who have severe night time symptoms over 24 hours), using the Crono APO-go ambulatory pump.

Patient response to apomorphine is relatively quick, (within 30 minutes) and therefore assessment of response can be quickly made and then dosage can be adjusted to optimum response within hours. This allows transfer of care to be achieved quickly.

The apomorphine intermittent injection dose regimen is individually titrated according to the patient's symptom management. This may range from 1-5 intermittent subcutaneous injections daily.

Continuous infusion dose may range from 50-120mg daily, usually during waking hours only (12-16 hours a day). Therefore the rate is usually between 2mg/hour and 8.5mg/hour. Using the 5mg/ml prefilled syringes the usual rate is between 0.4ml/hour and 1.7ml/hour. The dose starts at the lower end and is gradually titrated upwards to control symptoms. Refer to the NICE guidance on Parkinson's for further information on apomorphine regimens. .

Thumb tack needles, e.g. Neria lines and orange butterfly needles are recommended by KCH for administration of apomorphine infusion.

Duration of treatment

Long term

Criteria for stopping treatment

Significant side effects, lack of response at adequate doses, as determined by the consultant, Parkinson's Disease Nurse Specialist (PDNS), and the patient.

Monitoring Requirements including frequency

Consultant/Parkinson's Disease Nurse Specialist:

Before Treatment

A baseline ECG will be done on admission. An apomorphine challenge will be carried out by the PDNS and consultant measuring UPDRS part 3 to assess motor function, measurement of non-motor symptoms (NMSS or NMSQuest) baseline lying and standing blood pressure and timed walk if possible.

Once stable

§ In addition to assessment of effect of treatment on quality of life and non-motor assessments (using NMSS or NMSQuest), a repeat UPDRS part 3 will be performed on each visit to monitor motor progression of Parkinson's
§ To review and act upon abnormal blood results and advise GP on next steps

GP:

If in agreement to complete baseline ECG and forward results to KCH.
If ECG is normal and GP in agreement to prescribe domperidone 10mg TDS for 72 hours pre-attendance at KCH for initiation of APO-go® (apomorphine).

- To report any concerns about side-effects (possible allergic reactions, excessive somnolence, dizziness), co-morbidities (seizures, severe cardiovascular disease, mental illness), pregnancy, overuse or lack of efficacy to the Parkinson's specialist team (PDNS nurse or consultant)
- Report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk

Once stable:

- To refer any skin complaints around the injection site to the PDNS (See below practical issues for further information). If skin complaints are reported the PDNS will organize a nurse to visit the patient to provide further advice regarding minimization of local reactions.
- To take a full blood count at least every 6 months and report any abnormalities to the secondary care team.
- Haemolytic anaemia and thrombocytopenia will require referral back to the specialist for specialist care
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Follow up arrangements

Consultant/Specialist team:
After a successful challenge, the initiation, titration and adjustment of oral PD therapy will be managed by the PDNS following discussion with the Consultant and in accordance with the clinical management plan.

The specialist team will provide training, support and advice for General Practitioners, Community Pharmacists, District Nurses, the patient and family, aided by an APO-go® (apomorphine) community nurse available via helpline 24 hours a day. Patients will be reviewed at KCH initially three monthly and then six monthly thereafter. Continuing appropriateness of therapy will be reviewed at each appointment.

GP
The primary care team will be responsible for the ongoing prescribing of APO-go® (apomorphine), Neria lines and sharps bins once the patient has been stabilised on therapy and will continue to act as the primary contact for general healthcare.
To refer to specialist team if any significant developments or deterioration occur, such as occurrence of side effects, worsening of symptoms or inability to administer apomorphine.

All
Domperidone to be discontinued when patient is no longer nauseous and within two weeks.

Practical issues including other relevant advice/information

Reminder: this list is not exhaustive - for full details of adverse effects and all potential drug interactions refer to latest Summary of Product Characteristics (SPC) for the drug, available via www.medicines.org.uk.

The specialist team in secondary care provides the patient with information and advice about apomorphine therapy, including how to administer therapy and the devices used. This information is supported by written and audio information if required. Only when the patient and their family are satisfied with the process will treatment proceed.

It is important to minimise the development of nodules as it is thought that they may reduce absorption of apomorphine, thus reducing the efficacy of the treatment.

A clean technique is essential to minimise local reactions. It is important that patients, and those who care for them, are taught the correct technique for managing the infusion prior to initiation of apomorphine therapy. This training will be completed by the PDNS in secondary care. Ongoing support and further training will be available as needed from the PDNS and the APO-go® (apomorphine) community nurse.

Please note the following steps may help to reduce nodule formulation: (The patient and those who care for them will be trained in the following by the PDNS during in-patient initiation of therapy and training)

Daily rotation of injection sites.

Thumb tack needles, such as neria, should be sited slowly and gently into un-pinched skin at a 90-degree angle. When using this type of needle, it is important to hold on to the infusion line tube just above the head (tack) of the needle, to ensure full depth of insertion.

Gentle massaging of the injection sites on a daily basis, by hand or with a hand held massage device, could help to reduce nodule formation. Massage promotes healthy skin by encouraging good circulation to the adipose tissue whilst desloughing dead skin cells.

Silicone gel patches* are rarely required however can help to reduce nodule formation and relieve itchiness. The patches are placed over the nodules and left in place overnight. The patches can be used many times if they are rinsed in warm water and dried

carefully. Each packet contains instructions for use. It is not fully understood how these patches work to reduce nodule formation, although silica is known to exert a beneficial effect on scar tissue.

If pre-filled APO-go® (apomorphine) syringes are not available in primary care the specialist team should be contacted for advice.

Although doses up to 120mg daily are recommended by NICE, doses above 100mg are unlicensed.

Any problems with nodule formation should be referred to the specialist team

*Silicone gel patches should only be prescribed in exceptional circumstances on the advice of the supporting specialist. Any prescribeable silicone gel patch would be acceptable. For example: BAP Scarcare T, Cica Care, Ciltech or Dermatix (clear or fabric)

Summary of adverse effects	Adverse effect	Frequency	Management
(See Summary of Product Characteristics for full list www.medicines.org.uk) Very common: ≥1/10 Common: ≥1/100 to <1/10 Uncommon: ≥1/1000 to <1/100 Rare: ≥1/10,000 to <1/1000 Very rare: <1/10,000 Not known: cannot be estimated from available data	Nausea and vomiting	Common (mainly in DA naïve patients)	Domperidone 10mg three times daily to be started 72 hours prior to hospital admission. Treatment prescribed by consultant team, or by the GP depending on agreement and patient preference. To be continued until established on therapy; then gradually withdrawn over two weeks on advice of specialist team/consultant.
	Dyskinesia	Uncommon	Treatment to be adjusted or discontinued by PDNS following discussion with consultant.
	Sedation	Common	Usually transient at the start of therapy. Should resolve over the few first weeks. Treatment to be adjusted or discontinued by PDNS following discussion with consultant.
	Confusion and visual hallucinations	Common	Usually mild and transient. More commonly reported in patients with a history of neuropsychiatric complications induced by L-dopa (as co-beneldopa/co-careldopa) and/or dopamine agonists. If symptoms persist, attempts should be made to identify contributing factor under direct supervision of hospital team.
	Impulse control disorders including, but not limited to - Pathological gambling, increased libido, hypersexuality	Not known	Reversible on dose reduction or treatment discontinuation under supervision of consultant/PDNS.
	Injection site reactions (mild nodules to painful hard nodules) (skin ulceration)	Very common Uncommon	Refer to PDNS for advice – see practical issues section for information on minimising skin reactions.

Information provided to the patient

A copy of the clinical management plan will be sent to the patient in addition to the GP.

Patient information booklets and DVDs are also available from Genus pharmaceuticals via their website (www.apo-go.co.uk) including:

APO-go PEN set up guide – May 2017
APO-go PUMP set up guide – May 2017
APO-go skin care booklet – May 2017
APO-go pump programming guide – May 2017

Evidence Base for treatment and key references

1. National Institute for Health and Clinical Excellence (2006) **Parkinson's Disease: Diagnosis and management in primary and secondary care.** Department of Health, London. https://www.nice.org.uk/guidance/cg35
2. Claudia Trenkwalder, K.Ray Chaudhuri, Pedro J. García Ruiz, Peter LeWitt, Regina Katzenschlager, Friederike Sixel-Döring, Tove Henriksen, Ángel Sesar, Werner Poewe, Mary Bakerk, [...], Stuart Isaacsonr, Teus van Laars, Andrew Leest, Simon Lewisu, Juan Carlos Martínez Castrillov, Pablo Martinezmartinw, Per Odinx, John Osullivany, Georgios Tagarisz, Karoline. Expert Consensus Group Report on the use of apomorphine in the treatment of Parkinson's disease – clinical practice recommendations Parkinsonism & Related Disorders 06/2015; DOI:10.1016/j.parkreldis.2015.06.012
3. Bhidayasiri R, Chaudhuri KR, LeWitt P, Martin A, Boonpang K, van Laar T. Effective delivery of apomorphine in the management of Parkinson disease: practical considerations for clinicians and Parkinson nurses. Clin Neuropharmacol. 2015 May-Jun;38(3):89-103. doi: 10.1097/WNF.0000000000000082
4. Dewey, R.B., Hutton, T., LeWitt, A., Factor, S.A. (2001) **A randomised, double blind, placebo – Controlled trial of subcutaneously injected Apomorphine for Parkinsonian Off state events.** *Arch. Neurology*2001; 58: 1385– 1392.
5. Lees AJ, Stibe CM, Kempster PA, Stern GM; (1989) **Long-Term Use of Continuous or Intermittent Subcutaneous Administration of Apomorphine in the Management of L-Dopa-Induced Motor Oscillations;** Neurology; 1989; 39 (1): 365
6. Tyne HL, Parsons J, Sinnott A, Fox SH, Fletcher NA, Steiger MJ; 2004; **A 10 year retrospective audit of long-term apomorphine use in Parkinson's disease;** 2004; J Neurol; 251: 1370-1374

Katzenschlager R, Poewe W, Rascol O, Trenkwalder C, Deuschl G, Chaudhuri KR, Henriksen T, van Laar T, Spivey K, Vel S, Staines H. Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial. The Lancet Neurology. 2018;17(9):749-59.

4. COMMUNICATION AND SUPPORT

King's College and Princess Royal Hospitals switchboard: 0203 299 9000	
Consultant/specialist team Professor K Ray Chaudhuri Consultant and Director Parkinson's Centre of Excellence at Kings Miriam Parry (Senior Movement Disorders Nurse Specialist- Denmark Hill site)	Secretary: Enoka Suriyapperuma Tel: 02032999000 ext: 38336 Tel:02032999000 ext: 37773 Email: Miriamparry@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Shelley Jones (Consultant Pharmacist, Neurosciences) and the KCH Neuroscience pharmacy team	Tel: 02032999000 ext: 35717 Email: kch-tr.neuropharmacy@nhs.net
Oxleas NHS Foundation Trust switchboard: 020 8302 2678	
Specialist team: Sue Phillips **(**Parkinson's Nurse Specialist)	Tel: 0208 308 3227 Email: sue.phillips2@nhs.net
Community Apomorphine Nurse/ 24 Hour Helpline	Tel: 0844 880 1327