Effective Shared Care Agreement (ESCA)

Apomorphine

ESCA: For the treatment of motor fluctuations ('on-off' phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of apomorphine for Parkinson's disease can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are 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.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with Parkinson's disease are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. Confirm the diagnosis of Parkinson's disease
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made
4. Do baseline monitoring prior to initiation of apomorphine
5. Initiate treatment and stabilise dose of apomorphine
6. Review the patient's condition and monitor response to treatment regularly
7. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay
8. Report serious adverse events to the MHRA
9. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below)

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days						
2. Prescribe apomorphine at the dose recommended						
3. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
4. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist						
5. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment						
6. Refer back to specialist if condition deteriorates						
7. Report serious adverse events to specialist and MHRA						
8. Stop treatment on advice of specialist						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment
2. Share any concerns in relation to treatment with apomorphine with the specialist, clinical nurse specialist or GP
3. Report any adverse effects to the specialist or GP whilst taking apomorphine
4. Attend regular outpatient appointments with the specialist
5. Only make changes to apomorphine dosage as advised by healthcare practitioners

BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

SUPPORTING INFORMATION

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

Dosage and Administration

Selection of Patients Suitable for apomorphine:-

- 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.
- It is essential that the patient is established on domperidone, usually 20 mg three times daily for at least two days prior to initiation of therapy.
- Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist). The patient's treatment with levodopa, with or without dopamine agonists, should be optimised before starting apomorphine treatment.
- Apomorphine must not be used via the intravenous route.
- Do not use if the solution has turned green. The solution should be inspected visually prior to use. Only clear, colourless and particle free solution should be used.

APO-go PEN 10 mg/ml Solution for Injection	**APO-go AMPOULES 10 mg/ml Solution for Injection or Infusion**	**APO-go PFS 5mg/ml Solution for Infusion in Pre-filled Syringe**
APO-go Pen 10mg/ml Solution for Injection is for subcutaneous use by intermittent bolus injection.	APO-go Ampoules 10 mg/ml Solution for Injection or Infusion is for subcutaneous use by intermittent bolus injection. APO-go Ampoules 10 mg/ml Solution for Injection or Infusion may also be administered as a continuous subcutaneous infusion by minipump and/or syringe-driver .	APO-go PFS 5mg/ml Solution for Infusion in Pre-filled Syringe is a pre-diluted pre-filled syringe intended for use without dilution as a continuous subcutaneous infusion by minipump and / or syringe-driver. It is not intended to be used for intermittent injection.
Determination of the threshold dose. The appropriate dose for each patient is established by incremental dosing schedules. The following schedule is suggested: 1mg of apomorphine HCl (0.1ml), that is approximately 15-20 micrograms/kg, may be injected subcutaneously during a hypokinetic, or 'off' period and the patient is observed over 30 minutes for a motor response. If no response, or an inadequate response, is obtained a second dose of 2 mg of apomorphine HCl (0.2ml) is injected subcutaneously and the patient observed for an adequate response for a further 30 minutes. The dosage may be increased by incremental injections with at least a forty minute interval between succeeding injections, until a satisfactory motor response is obtained.		*Determination of Threshold Dose* The threshold dose for continuous infusion should be determined as follows: Continuous infusion is started at a rate of 1 mg apomorphine HCl (0.2 ml) per hour then increased according to the individual response each day. Increases in the infusion rate should not exceed 0.5 mg at intervals of not less than 4 hours. Hourly infusion rates may range between 1mg and 4mg (0.2ml and 0.8ml), equivalent to 0.014 – 0.06 mg/kg/hour. Infusions should run for waking hours only. Unless the patient is experiencing severe night-time problems, 24 hour infusions are not advised. Tolerance to the therapy does not seem to occur as long as there is an overnight period without treatment of at least 4 hours. In any event, the infusion site should be changed every 12 hours. Patients may need to supplement their continuous infusion with intermittent bolus boosts, as necessary, and as directed by their physician. A reduction in dosage of other dopamine agonists may be considered during continuous infusion.

Establishment of treatment. Once the appropriate dose is determined a single subcutaneous injection may be given into the lower abdomen or outer thigh at the first signs of an 'off' episode. It cannot be excluded that absorption may differ with different injection sites within a single individual. Accordingly, the patient should then be observed for the next hour to assess the quality of their response to treatment. Alterations in dosage may be made according to the patient's response. The optimal dosage of apomorphine hydrochloride varies between individuals but, once established, remains relatively constant for each patient. *Precautions on continuing treatment.* The daily dose of APO-go varies widely between patients, typically within the range of 3-30mg, given as 1-10 injections and sometimes as many as 12 separate injections per day. It is recommended that the total daily dose of apomorphine HCl should not exceed 100mg and that individual bolus injections should not exceed 10mg. In clinical studies it has usually been possible to make some reduction in the dose of levodopa; this effect varies considerably between patients and needs to be carefully managed by an experienced physician. Once treatment has been established domperidone therapy may be gradually reduced in some patients but successfully eliminated only in a few, without any vomiting or hypotension.		*Establishment of treatment.* Alterations in dosage may be made according to the patient's response. The optimal dosage of apomorphine hydrochloride varies between individuals but, once established, remains relatively constant for each patient. *Precautions on continuing treatment* The daily dose of APO-go varies widely between patients, typically within the range of 3-30 mg. It is recommended that the total daily dose of apomorphine HCl should not exceed 100 mg. In clinical studies it has usually been possible to make some reduction in the dose of levodopa; this effect varies considerably between patients and needs to be carefully managed by an experienced physician. Once treatment has been established domperidone therapy may be gradually reduced in some patients but successfully eliminated only in a few, without any vomiting or hypotension
	APO-go AMPOULES 10 mg/ml Solution for Injection or Infusion	**APO-go PFS 5mg/ml Solution for Infusion in Pre-filled Syringe**
	Continuous Infusion Patients who have shown a good 'on' period response during the initiation stage of apomorphine therapy, but whose overall control remains unsatisfactory using intermittent injections, or who require many and frequent injections (more than 10 per day), may be commenced on or transferred to continuous subcutaneous infusion by minipump and/or syringe driver as follows:- Continuous infusion is started at a rate of 1 mg apomorphine HCl (0.1 ml) per hour then increased according to the individual response. Increases in the infusion rate should not exceed 0.5 mg per hour at intervals of not less than 4 hours. Hourly infusion rates may range between 1 mg and 4 mg (0.1 ml and 0.4 ml), equivalent to 0.015 - 0.06 mg/kg/hour. Infusions should run for waking hours only. Unless the patient is experiencing severe night-time problems, 24 hour infusions are not advised. Tolerance to the therapy does not seem to occur as long as there is an overnight period without treatment of at least 4 hours. In any event, the infusion site should be changed every 12 hours. Patients may need to supplement their continuous infusion with intermittent bolus boosts, as necessary, and as directed by their physician. A reduction in dosage of other dopamine agonists may be considered during continuous infusion.	*Continuous Infusion* Patients who have shown a good 'on' period response during the initiation stage of apomorphine therapy, but whose overall control remains unsatisfactory using intermittent injections, or who require many and frequent injections (more than 10 per day), may be commenced on or transferred to continuous subcutaneous infusion by minipump and / or syringe driver as follows:- The choice, of which minipump and / or syringe-driver to use, and the dosage settings required, will be determined by the physician in accordance with the particular needs of the patient.

Children and adolescents: - Contraindicated for children and adolescents under 18 years of age	
Elderly: The elderly are well represented in the population of patients with Parkinson's disease and constitute a high proportion of those studied in clinical trials of apomorphine. The management of elderly patients treated with apomorphine has not differed from that of younger patients. However, extra caution is recommended during initiation of therapy in elderly patients because of the risk of postural hypotension.	
Renal Impairment	No dose adjustment required
Hepatic impairment	Apomorphine is contraindicated in patients with hepatic insufficiency
Contra-indications / Special precautions	**Contraindication:-** In patients with respiratory depression, dementia, psychotic diseases or hepatic insufficiency. Apomorphine HCl treatment must not be administered to patients who have an 'on' response to levodopa which is marred by severe dyskinesia or dystonia. Apomorphine should not be administered to patients who have a known hypersensitivity to apomorphine or any excipients of the medicinal product. Apomorphine is contraindicated for children and adolescents under 18 years of age. **Cautions:-** Apomorphine HCl should be given with caution to patients with renal, pulmonary or cardiovascular disease and persons prone to nausea and vomiting. Extra caution is recommended during initiation of therapy in elderly and/or debilitated patients. Since apomorphine may produce hypotension, even when given with domperidone pre-treatment, care should be exercised in patients with pre-existing cardiac disease or in patients taking vasoactive medicinal products such as anti-hypertensives, and especially in patients with pre-existing postural hypotension. Since apomorphine, especially at high dose, may have the potential for QT prolongation, caution should be exercised when treating patients at risk for torsades de pointes arrhythmia. Apomorphine is associated with local subcutaneous effects. These can sometimes be reduced by the rotation of injection sites or possibly by the use of ultrasound (if available) in order to avoid to areas of nodularity and induration. Haemolytic anaemia and thrombocytopenia have been reported in patients treated with apomorphine. Haematology tests should be undertaken at regular intervals as with levodopa, when given concomitantly with apomorphine. Caution is advised when combining apomorphine with other medicinal products, especially those with a narrow therapeutic range . Neuropsychiatric problems co-exist in many patients with advanced Parkinson's disease. There is evidence that for some patients neuropsychiatric disturbances may be exacerbated by apomorphine. Special care should be exercised when apomorphine is used in these patients. Apomorphine has been associated with somnolence and episodes of sudden sleep onset, particularly in patients with Parkinson's disease. Patients must be informed of this and advised to exercise caution whilst driving or operating machines during treatment with apomorphine. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Furthermore, a reduction of dosage or termination of therapy may be considered. *Impulse control disorders* Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including apomorphine. Dose reduction/tapered discontinuation should be considered if such symptoms develop. Apomorphine solution for injection/infusion contains sodium bisulphite which may rarely cause severe allergic reactions and bronchospasm. This medicinal product contains less than 1 mmol sodium (23 mg) per 10ml, i.e. essentially “sodium-free”.

<table>
<tr><td rowspan="2">Side Effects</td><td>Very common</td><td>Most patients experience injection site reactions, particularly with continuous use. These may include subcutaneous nodules, induration, erythema, tenderness and panniculitis. Various other local reactions (such as irritation, itching, bruising and pain) may also occur</td></tr>
<tr><td>Common</td><td>Neuropsychiatric disturbances, somnolence, dizziness / light-headedness, yawning, nausea and vomiting. Transient sedation with each dose of apomorphine HCl at the start of therapy may occur; this usually resolves over the first few weeks.</td></tr>
<tr><td>Monitoring</td><td colspan="2">FBC
U&E</td></tr>
<tr><td>Drug Interactions (highlighted interaction are the significant ones)</td><td colspan="2">Apomorphine has the following interaction information:
<table>
<tr><td>Antipsychotics</td><td>effects of apomorphine antagonised by antipsychotics
Note: Increased risk of toxicity with myelosuppressive drugs</td></tr>
<tr><td>Entacapone</td><td>effects of apomorphine possibly enhanced by entacapone</td></tr>
<tr><td>Ondansetron</td><td>possible increased hypotensive effect when apomorphine given with ondansetron —avoid concomitant use</td></tr>
</table>
Apomorphine belongs to Dopaminergics and will have the following interactions:
<table>
<tr><td>Memantine</td><td>effects of dopaminergics possibly enhanced by memantine</td></tr>
<tr><td>Methyldopa</td><td>antiparkinsonian effect of dopaminergics antagonised by methyldopa</td></tr>
</table></td></tr>
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References

Apomorphine SmPC
Apomorphine BNF
NICE CG 35 - Parkinson's disease: Diagnosis and management in primary and secondary care

I agree to participate in this shared care agreement for the treatment of the below named patient with apomorphine for Parkinson's disease

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: