Gloucestershire Hospitals
NHS Foundation Trust

The use of Apomorphine in Parkinson's disease:

Treatment Guideline

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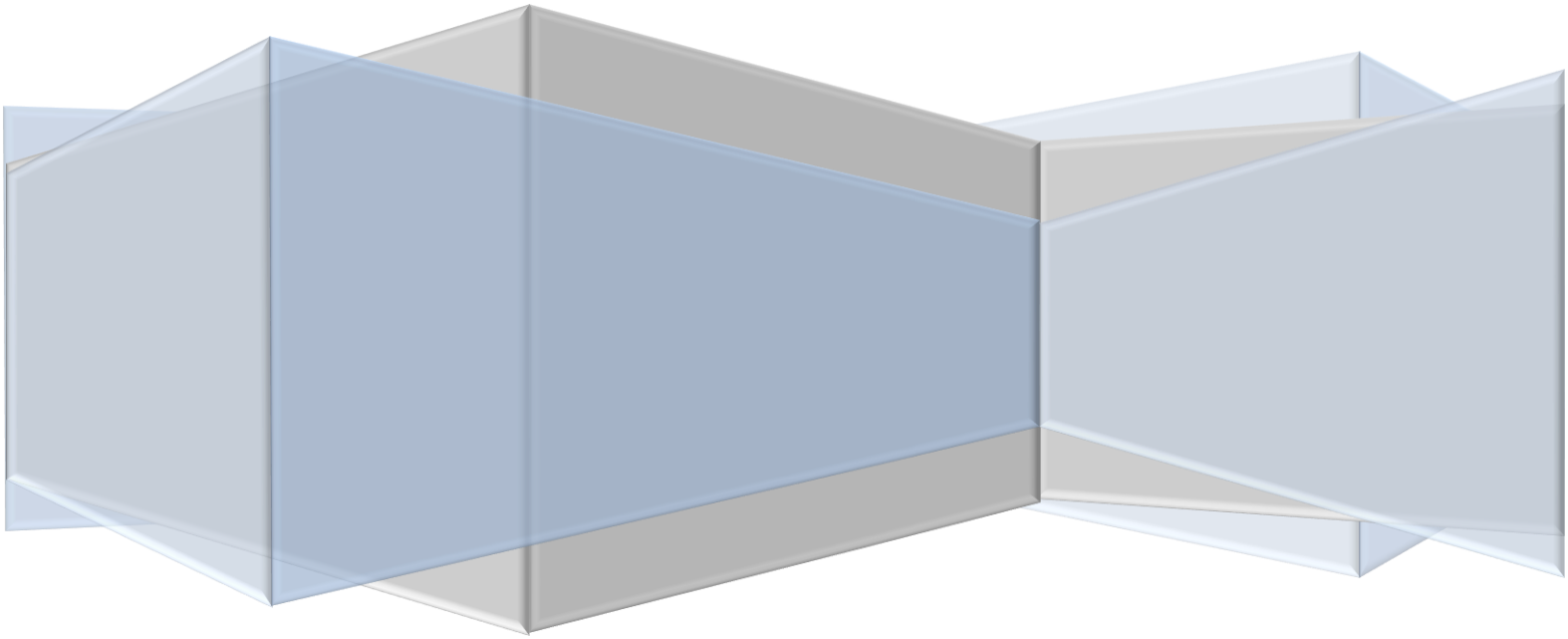

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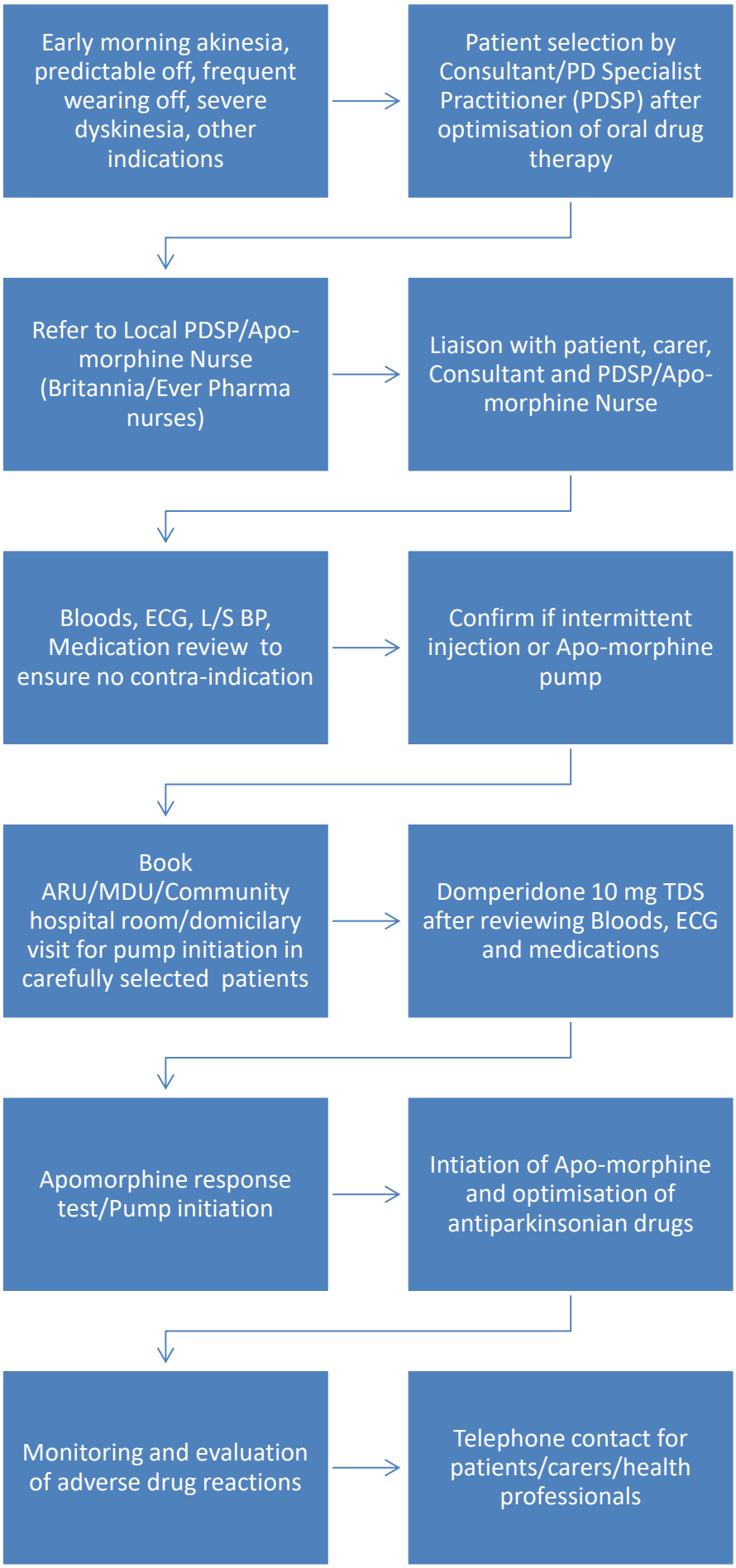
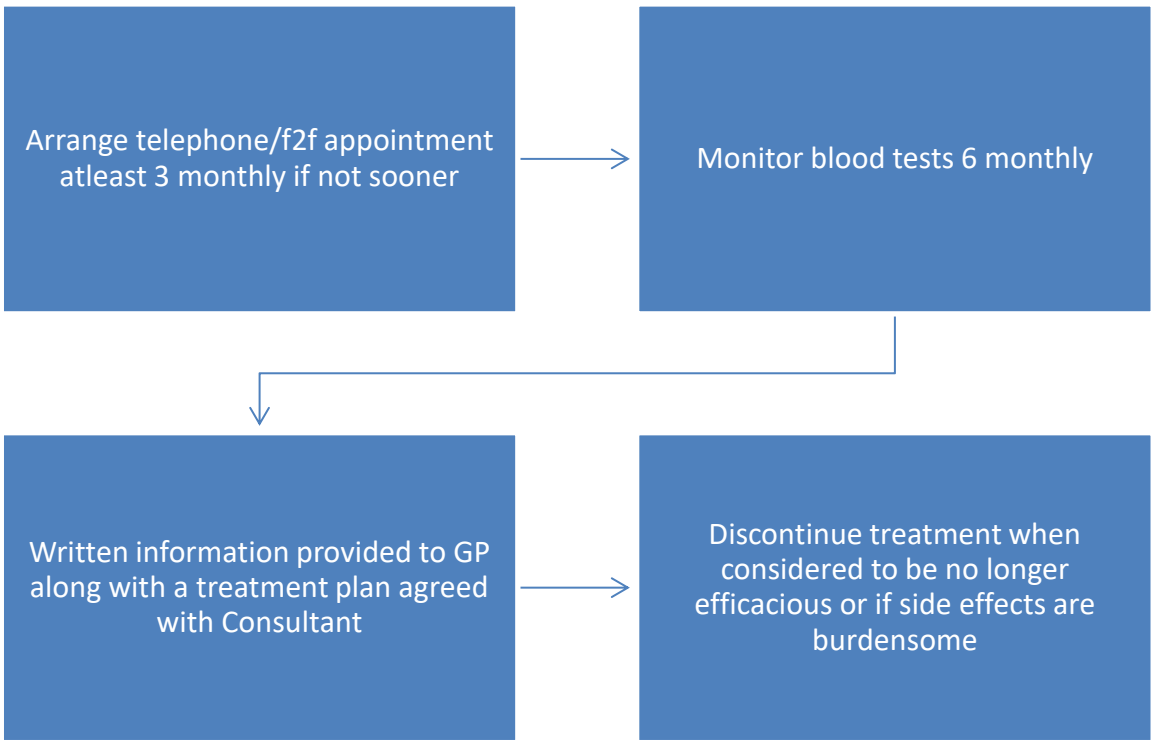

Early morning akinesia, predictable off, frequent wearing off, severe dyskinesia, other indications
Patient selection by Consultant/PD Specialist Practitioner (PDSP) after optimisation of oral drug therapy
Refer to Local PDSP/Apo-morphine Nurse (Britannia/Ever Pharma nurses)
Liaison with patient, carer, Consultant and PDSP/Apo-morphine Nurse
Bloods, ECG, L/S BP, Medication review to ensure no contra-indication
Confirm if intermittent injection or Apo-morphine pump
Book ARU/MDU/Community hospital room/domicilary visit for pump initiation in carefully selected patients
Domperidone 10 mg TDS after reviewing Bloods, ECG and medications
Apomorphine response test/Pump initiation
Intiation of Apo-morphine and optimisation of antiparkinsonian drugs
Monitoring and evaluation of adverse drug reactions
Telephone contact for patients/carers/health professionals


Arrange telephone/f2f appointment atleast 3 monthly if not sooner
Monitor blood tests 6 monthly
Written information provided to GP along with a treatment plan agreed with Consultant
Discontinue treatment when considered to be no longer efficacious or if side effects are burdensome

Foreword

These guidelines provide information on the use of Apomorphine in patients with Parkinson's disease (PD). Apomorphine is a dopamine agonist administered subcutaneously for the treatment of Parkinson's disease.

This document has been adapted from the Cwm Taf Morgannwg University Health Board "The Use of Apomorphine in Parkinson's disease: Shared Care Guideline" with their kind permission. It has been produced as a source of information for all health professionals providing care of patients with PD within Gloucestershire Hospitals NHS Foundation Trust and Gloucestershire Care Services. The document aims to identify lines of communication between primary and secondary care and explain the responsibilities of all those involved in the different aspects and stages of treatment.

The owning division for this document is Medicine and the owning specialities are Care of the Elderly and Neurology.

This document has been reviewed earlier than intended due to various reasons: change in service provision, emerging clinical need, availability of additional brand of Apomorphine and COVID-19 pandemic. Gloucestershire is a large county. GHFT is a two-site district general hospital located in the centre of this county. Over 50% of the population live outside in the periphery of this region which is served by 7 community hospitals. It provides a useful opportunity to extend the provision of Apomorphine beyond acute hospitals. For a carefully selected group there is a distinct need for offering Apomorphine pump initiation in the patient's own home.

There is an intention to review it in 2 years or sooner depending upon clinical developments.

Professionals involved in the consultation of the document are PD Specialist Practitioners, Consultant Geriatricians, Consultant Neurologists and Pharmacists.

Introduction

Parkinson's disease is the second most common neurodegenerative disorder with a prevalence of about 160/100,000 and annual incidence of 15-20/100,000. It is more common in the older population and slightly more prevalent in males. Exact aetiology is unknown but is felt to be linked to loss of dopaminergic neurons. It is a progressive illness associated with motor fluctuations in the complex and later stages. Fluctuations involve loss of motor control and dyskinesia which can become disabling and lead to weight loss, falls and increasing frailty.

Levodopa with or without other oral/transdermal dopamine agonists provides good control in the early stages. In later stages "off "periods can be associated with dystonia, depression, pain, sleep dysfunction, bladder dysfunction and swallowing difficulties. Apomorphine has been shown in several open label studies, to significantly reduce and sometimes reverse these "off" periods. The National Institute for Care Excellence states Apomorphine is an option for best medical therapy in advanced Parkinson's disease. Control of these symptoms can be challenging and Apomorphine provides an additional option to best medical oral therapy before considering other advanced therapies such as Deep Brain stimulation or Levodopa-carbidopa intestinal gel.

This document outlines the process of identifying individuals suitable for Apomorphine, initiation and subsequent management.

Key objectives of the guideline

1. To provide primary and secondary care teams with information on the use of Apomorphine therapy in the treatment of Idiopathic Parkinson's disease.

2. To provide a framework for co-operation and understanding between the primary care team and the hospital, so that Apomorphine (and other anti-Parkinson's therapy) can be monitored and adjusted according to patients' needs.

3. To establish clear lines of communication between general practitioners, community pharmacists, community hospitals, hospital pharmacists, district nurses and other members of the multidisciplinary team.

4. Other policies that need to be considered are Non-medical prescribing policy, POPAM, Consent to examination or treatment policy, Home care policy and Waste management policy.

Presentation of pen/pump

There are currently two brands of Apomorphine available, Dacepton® and Apo-Go®. Infusion pumps and pen devices are not interchangeable. Patients should be maintained on the same one unless a decision is made to switch, with patient and carer retraining.

Pen devices

- Dacepton cartridge 10mg/ml (30mg/3ml) for use in multiuse D-Mine Pen. One cartridge has an in-use expiry of 15 days after first opening. Supplied in packs of 5 cartridges. Dacepton pen should be primed in between every dose to ensure a full dose is administered each time.
- Apo-go prefilled disposable pen 10mg/ml (30mg/3ml). One pen has an in-use expiry of 48 hours after first opening. Supplied in packs of 5 pens. Needles are provided free of charge.

Solution for infusion (via pump)

Dacepton vial 5mg/ml (100mg/20ml). Supplied in packs of 5 vials. Dacepton pump requires a new reservoir each time to load each 20ml vial

- Apo-go prefilled syringes 5mg/ml (50 mg/10ml). Supplied in packs of 5 prefilled syringes. Consumables: plastic syringes and connectors are dispatch with every PFS order and are provided free of charge. Infusion lines are an additional prescription item.

Apo-go pen

APO-GO PUMP

D-mine Pump **D-mine pen**

Apomorphine therapy

Apomorphine has been licensed since 1993 for use in patients with disabling motor fluctuations who are inadequately controlled with levodopa or dopamine agonists. The licence covers both subcutaneous intermittent injections and continuous subcutaneous infusions.

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.

1. Apomorphine may be administered as a "rescue therapy" with intermittent subcutaneous bolus injections given via a pen. Either Apo-go pen or D-mine pen.
2. For those patients who experience more complex motor fluctuations, including dyskinesias, a continuous subcutaneous infusion using an ambulatory pump. Either an APO-go pump may be used with the APO-go PFS, or D-mine pump with cartridges.

In carefully selected patients who respond to the drug, Apomorphine pen can provide a means of *rescue* within 5–10 minutes of administration, thereby regaining mobility and independence. The effect usually lasts for about an hour. Apomorphine can improve quality of life and may keep patients out of costly institutional care for many years.

The dose of Apomorphine is carefully titrated on an individual basis and can range from a few milligrams daily by intermittent subcutaneous injections, up to 100 mg daily by continuous infusion.

Apomorphine response test

Before therapy can be initiated an Apomorphine response test is necessary to:

1. Determine whether a patient has a positive response to the medication.
2. Observe the patient for side effects such as nausea, vomiting, postural hypotension, hallucinations.

Three days prior to the challenge, Domperidone 10 orally three times a day (tds) can be commenced (at home) to avert the significant emetic effects of Apomorphine. The patient can have the response test in a variety of settings (day case in acute /community hospital) depending on the local service provision, clinical need, and patient choice. It is important that the response is performed in a safe environment.

Britannia and Ever Pharma appoint specialist Apo-morphine nurses and they have an honorary contract with Gloucestershire Hospitals NHS Foundation Trust. These nurses would be henceforth referred to as Apo-morphine nurses within the document.

Procedure

1. ECG is performed to exclude cardiac conduction problems or significant cardiac disease. QTc >450mms in men and 470 mms in women is a contraindication. If abnormalities are present, the response test will not take place and the patient will be referred to a cardiologist for possible further investigation.
2. Pre-treatment with Domperidone 10 tds is commenced for 72 hours prior to the challenge. It is prescribed by specialist team, obtained via the GP surgery or hospital pharmacy.
3. Ideally the patient should not receive any oral anti-Parkinson medication for a minimum of eight hours prior to the challenge, to provoke an “off” state. Test should preferably be carried out in the morning. Patient is advised to bring in their first dose but not take it. If the test is being carried out in the afternoon, last dose should have been taken 4-6 hours prior to the test. Patient's mobility should be considered if the challenge is to be performed as a day case. Dispersible Madopar can be given or the patients first dose of levodopa to enable them to attend the clinic setting.
4. The PD Specialist Practitioner or Apomorphine nurse is responsible for arranging and administering Apo-morphine response test.
5. Motor function is assessed at baseline by PDSP or the Apo-morphine nurse using the Unified Parkinson’s Disease Rating Scale (UPDRS) section III Motor Function together with a timed a 12-metre walk (the time it takes the patient to rise from a chair with arms folded then walk 6m, turn, return 6m, then sit down). Lying and standing blood pressure is also recorded due to the possible hypotensive effects of dopamine agonists. These assessments are repeated after sequential doses of Apomorphine.

6. 1mg Apomorphine is administered subcutaneously, and blood pressure repeated 15-20 minutes following this dose, monitored for side effects, and observed for a positive response. UPDRS, timed sit to stand and walk or timed hand movements are to be repeated every half an hour.

7. If there is no or a poor response, a subsequent dose of 2 mg Apomorphine is given. Assessments and observations are continued as above.

8. The dose is increased in incremental steps every 20-30 minutes (i.e., 1mg, 2mg, 3mg, and 5mg) and stopped when a positive response is seen. If at 7 mg there is no response, then the patient is termed a non-responder. If a mild response is noted at 7mg, it is up to the patient's PD Consultant as to whether the maximum dose of 10mg should be administered.

Positive Response Test

A response test is positive if either the following are seen:

1. A decrease in UPDRS motor score by at least 20%.

2. A minimum of 20% improvement in either timed hand tests or timed walking.

Treatment strategies

Intermittent subcutaneous injections

Intermittent subcutaneous injections are used as a *rescue* for patients who experience unpredictable disabling "off" periods and/or painful dystonia. These injections are often used in conjunction with oral therapy. The timing of each injection is crucial if an impending "off" period is to be averted (taking into consideration when the next oral levodopa dose is likely to take effect).

The individual effective dose is determined for each patient and is defined as being that which will reverse or avert an off period. Early symptoms of an approaching "off" period is individual to each patient. Common signs include curling or dystonic toes, bradykinesia, rigidity, cramp in the calf muscles and a sudden low mood by the patients. The injection is administered at the onset, or ideally, in anticipation of an "off" period.

Intermittent subcutaneous injections can be administered via:

- The pen device is discrete and easy to use and is set so a predetermined amount of Apomorphine (based on the response test) is administered at each '*rescue'* injection. Injections are given subcutaneously either into the lower abdominal wall, below the umbilicus, in the upper outer aspects of the thighs, or the upper arms. The injection site is rotated for each injection to avoid irritation of the skin.

For instructions on how to use the pen refer to the appropriate patient information leaflet.

Continuous subcutaneous infusion using Apomorphine syringe pump.

The continuous infusion ambulatory pump is used for patients that have shown a good 'on' response to the drug but whose overall control remains unsatisfactory using intermittent injections. Alternatively, patients who require frequent injections (6-8 per day) may be transferred to a continuous infusion administered via a pump to reduce potential problems with injection sites and cost. Some patients are initiated on a pump without first trying intermittent injections. Such as those patients experiencing disabling and exhausting dyskinesia, who may also benefit from a continuous infusion, as it may allow their oral levodopa medication to be reduced. Experience has found that

managing this group of patients on a combination of Apomorphine and oral dopamine agonists and subsequently reducing oral levodopa can dramatically reduce dyskinesia. It is thought a 30% reduction in levodopa can be made almost immediately once an infusion is commenced.

Both Britannia Pharmaceuticals and Ever Pharma supply their pumps which are loaned to the patient along with specific syringes or cartridges, which fit the pump.

The dose and duration of the pump is individualised to patient need. Daily doses will not normally exceed 100mg, though in rare cases higher daily doses have been used. The duration of the infusion is usually throughout the waking day (for example 14 hrs) but on rare occasions the infusion may run over 24 hours.

Site of the infusion

The best site to insert the subcutaneous needle is the lower abdominal wall, below the umbilicus. However outer aspects of the thigh can be used. It is important to rotate the injection site daily to minimise the possibility of localised skin irritation. Ensure that the bevel of the needle is facing inwards.

Storage and stability

Both pre-filled Apo-go and Dacepton products should be stored at room temperature (at or below 25ºC) and protected from light. **Do not use if the solution is green or cloudy**.

Prescribing Apomorphine

Infusion rates for the APO-go ambulatory infusion pump (supplied by Britannia's Pharmaceuticals). Britannia suggest that a dose per hour is prescribed.

mg Apomorphine per hour	ml of diluted solution per hr (Flow rate)	Hours/minutes running time (100mg in 20ml syringe)	Hours/minutes running time (50mg in 20ml syringe*)
1.0	0.2		
1.5	0.3		
2.0	0.4		25.00
2.5	0.5		20.00
3.0	0.6		16.41
3.5	0.7		14.17
4.0	0.8	24.58	12.30
4.5	0.9	22.13	11.07
5.0	1.00	20.00	10.00
5.5	1.10	18.10	9.05
6.0	1.20	16.40	8.20
6.5	1.30	15.22	7.41
7.0	1.40	14.17	7.09
7.5	1.50	13.20	6.40
8.0	1.60	12.30	6.15
8.5	1.70	11.46	5.53
9.0	1.80	11.07	5.34
9.5	1.90	10.31	5.16
10.00	2.00	10.00	5.00

Obtaining Appliance supplies

Britannia Pharmaceuticals

APO-go Pump

Ambulatory Infusion Pump, dedicated 20ml syringes and connectors are supplied free of charge for use with APO-go PFS.

Ever Pharma

D-mine pump

Ambulatory infusion pump and infusion lines are supplied free of charge to be used with Dacepton reservoir. It is important to order the D-mine pump reservoirs on prescription form as part of the pump accessories needed.

Infusion Lines

Prescribed on FP 10 for Britannia only.

Neria lines:

78-060-2931	FSN131 Neria™ infusion set	60 cm.
78-110-2931	FSN132 Neria™ infusion set	110 cm.

Pre-initiation

Patient selection

Patients potentially suitable for treatment with Apomorphine will be identified by a consultant neurologist, care of the elderly consultant or Parkinson's Disease Specialist Practitioner (PDSP) following discussion with the patient's Parkinson's consultant. Patients must have an established diagnosis of Parkinson's disease in the complex phase of the condition with uncontrolled motor fluctuations and be under the care of a Consultant Neurologist or Care of the elderly Consultant.

Oral drug therapy with levodopa, with or without dopamine agonists, should be optimised before consideration of Apomorphine.

Patients being considered for treatment using intermittent injections 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.

Patients who are already being treated with intermittent injections of Apomorphine, who have shown a good 'on' period response during the initiation stage of Apomorphine therapy, but whose overall control remains unsatisfactory, or who require many and frequent injections (more than six per day), may be considered for continuous subcutaneous infusion.

Patients meeting above criteria will be referred to the PDSP/Apomorphine nurse to arrange and administer the response test/initiate the pump. A joint assessment in an outpatient clinic with the patient, carer, Consultant and PDNS/Apomorphine nurse to address questions arising as well as review bloods, ECG, potential drug interactions and side effects of Apo-morphine will be arranged. MHRA guidance requires ECG at baseline to exclude prolonged QTc interval (>450 mms in men and >470 mms in women).

A careful assessment will be made at this appointment to identify those who would benefit from home initiation of Apomorphine pump. This would depend upon clinical need, geographic location, patient preference, PDSP/Apomorphine nurse availability and the potential clinical risks. Dose administered via pump is at a much lower rate if initiated at home i.e., 0.5 mg/hour as against 1mg/hour. Home set up enables a gradual start to the treatment and allows patients and carers to get used to the pump before reducing doses of Dopamine agonists and Levo-dopa

Side effects

Usually, undesirable effects are observed within the first week after treatment and are temporary in nature. Undesirable effects may be related to the active substance, the injection procedure, or both.

The frequency of side effects is as follows:

Very common (≥1/10)

Common (≥1/100 to <1/10)

Uncommon (≥1/1,000 to <1/100)

Rare (≥1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from the available data)

Potential side effects that the patient should be alerted to include:

Very Common	**▪ Hallucinations**
Common	**▪ Injection reactions, particularly with continuous infusion. These may include subcutaneous nodules, induration, erythema, tenderness, and panniculitis. Various other local reactions (such as irritation, itching, bruising and pain) may also occur.** **▪ Nausea and vomiting, particularly when Apomorphine treatment is first initiated, usually because of the omission of Domperidone *** **▪ Transient sedation (usually resolves over the first few weeks).** **▪ Dizziness / light-headedness** **▪ Neuropsychiatric disturbances including transient mild confusion**

	▪ **Peripheral edema**
Uncommon	▪ **Local and generalised rashes** ▪ **Injection site ulceration** ▪ **Postural hypotension** ▪ **Sudden sleep onset episodes** ▪ **Dyskinesia during 'on' periods, which can be severe in some cases and in a few patients, may result in cessation of therapy.** ▪ **Hemolytic anemia and thrombocytopenia** ▪ **Positive Coombs' tests** ▪ **Breathing difficulties**

* Apomorphine is emetogenic and 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. In line with MHRA guidance 2016, this should be done under the following conditions:

https://www.gov.uk/drug-safety-update/apomorphine-with-domperidone-minimising-risk-of-cardiac-side-effects

Interactions

Even when co-administered with Domperidone, Apomorphine may potentiate the antihypertensive effects of these medicinal products.

Co-administration of Apomorphine with other drugs known to prolong the QT interval must be avoided.

The SPC for the Dacepton brand recommends that due to profound hypotension and loss of consciousness when Apomorphine was administered with ondansetron, the concomitant use of these is contraindicated.

For full list see SPC at www.medicines.org.uk/EMC and BNF.

Contraindications and warnings

Contra-indications

- In patients with respiratory depression, dementia, psychotic diseases, or hepatic insufficiency. Mild cognitive impairment is not a contra-indication.
- Apomorphine must not be administered to patients who have an “on” response to levodopa which is marred by severe dyskinesia or dystonia.
- Hypersensitivity to the active substance or to any of the excipients.
- Concomitant use of ondansetron due to the risk of QT prolongation, severe hypotension, and loss of consciousness (use contra- indicated - Dacepton brand)
- Contraindicated for children and adolescents under 18 years of age.

Cautions

- Apomorphine may cause hypotension. Use with caution in those with pre-existing cardiovascular disease, including pre-existing postural hypotension or if taking antihypertensive. It also has the potential for QT prolongation especially at high doses. Use with caution in patients at risk for torsade de pointes arrhythmia.
- Patients with renal or pulmonary disease.
- Patients prone to nausea and vomiting.

Therapy initiation

The patient will be provided with written information about the drug treatment and advised of the following:

▪ How Apomorphine is used (including the associated practicalities) and how it works.

▪ Potential side effects including the risk of impulse control disorder, dopamine dysregulation syndrome and hyper somnolence (refer to SPC guidelines). In the event of hyper somnolence, the patient must be informed to refrain from driving or engaging in activities (e.g. operating machines) where impaired alertness may put themselves or others at risk of serious injury or death until such recurrent episodes and somnolence have resolved.

▪ Anticipated level of symptom control.

▪ Home care delivery scheme and need for ongoing monitoring as advised by the specialist team.

Once a decision has been made for a challenge/infusion it is the responsibility of the PDSP to also liaise with the respective drug company to request a challenge pack to be delivered to the GRH pharmacy and/or delivery of a pump for administration of continuous infusion (if applicable).

On the day of the challenge the PDSP/Apo-morphine nurse will:

- Ensure the patient has taken the prescribed loading dose of Domperidone.
- Ensure the patient has stopped dopaminergic medication as previously advised (minimum of four hours unless otherwise indicated) to induce an “off” state.
- Ensure the individual is aware of the potential side effects (see SPC guidelines).
- Re-establish verbal consent from patient as per Trust policy.
- Undertake baseline patient assessments prior to the first injection of Apomorphine as follows:
  - UPDRS section III
  - Postural blood pressure readings
  - Pulse
  - Respiratory rate
  - Timed walk using the 6 metre “up and go” test

Intermittent injections

▪ 1mg/0.1ml of Apomorphine (10mg/1ml) injected subcutaneously as a bolus injection in the lower abdomen or outer thigh, during a hypokinetic, or 'off' period
▪ Observe the patient over a maximum of 30 minutes for a motor response
▪ Assessment of UPDRS section III, postural blood pressure, pulse and respiratory rate, timed walk should be repeated at 30 minutes or sooner if there is a visible clinical response at the discretion of the clinician undertaking the challenge (a minimum of 15 minutes post injection).
▪ If no response, or an inadequate response is obtained, a second dose of 2 mg of Apomorphine (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 of 2mg up to a maximum of 10mg with at least a forty-minute interval between succeeding injections, until a satisfactory motor response is obtained, the challenge is abandoned due to side effects or there is a lack of response.

Continuous subcutaneous infusion

Start infusion at a rate of 1mg (0.2ml) Apomorphine per hour. The infusion should run during waking hours only (approximately 16 hours), unless the patient is experiencing intrusive nighttime symptoms, a 24-hour infusion is not advised.
▪ An hour after initiation the following investigations will be undertaken by the PDNS:
• UPDRS section III
• Postural blood pressure readings
• Pulse
• Respiratory rate

The hourly infusion rate may range between 1mg and 4mg (0.2ml and 0.8ml).

The total daily dosage should not exceed 100mg/24hours.

During the procedure it is the responsibility of the PDSP to teach the patient and carer (if applicable), how to use the Apomorphine penject device or Apomorphine pump and how to administer Apomorphine using either of these devices (as appropriate) as per manufacturing guidelines.

Stopping the challenge/process of incremental infusion
The challenge will be stopped if a positive response is achieved or a dose of 10mg is reached with no positive response. A positive response is defined as follows:

- An improvement in UPDRS score of 20% of baseline score
- More than 25% improvement in walking time using a 6-metre timed up and go test.

- Alleviation of specific symptoms, e.g., pain, dystonia, non-motor presentations such as urinary retention, gastric disturbances, anxiety

The challenge will be stopped in the event of any side effects as detailed above in the relevant section.

The challenge may also be stopped in the event of excessive dyskinesia as deemed by the patient and/or PDNS.

If a positive response is obtained in the absence of any significant side effects, and the PDSP/Apomorphine nurse is satisfied the patient can safely self-administer Apomorphine, the patient will be discharged with four weeks of Apomorphine, in accordance with POPAM. Subsequent prescriptions will be provided by the hospital via the home care delivery scheme providing the patient agrees.

Prior to discharge the patient will be advised of the following:
• The need to report any adverse effects to the Parkinson's specialist team

• The plan for follow up and the need to attend regular out-patient reviews as directed by the specialist team to ensure safe prescribing and on-going supply of Apomorphine prescriptions via home care delivery scheme

▪ For female patients, the need to notify the Parkinson's specialist team if they are attempting to conceive or discover that they are pregnant
▪ Appropriate advice on storage and handling
▪ How to contact the Parkinson's specialist team
▪ How to restart oral Parkinson's medication and how to withdraw Domperidone
▪ The importance of skin site monitoring and rotating the injection/infusion site regularly.

The result of the challenge or infusion will be communicated to the referring Consultant and the GP by the PDSP/Apomorphine nurse in written format and a follow up appointment will be arranged with the Consultant within 3 months. Further follow up appointments would be dictated by the nature of response and tolerability.

Post initiation

Telephone follow- up by the PDSP/Apomorphine nurse within a week or sooner will be arranged. A face-to-face appointment within a month with the PDSP and 3 monthly follow-ups with the Consultant will be arranged. A medication plan should be agreed with the Consultant with a view to reducing doses of Dopamine agonist or Levodopa medications. It is anticipated that there will be a 30% reduction in the dose of Levodopa.

Bloods including FBC, Coombe's test will be arranged every 6 months. ECG will be repeated only if patient reports any cardiac symptoms such as syncope or palpitations.

Apo-morphine challenge may not be successful in a few patients. They should be offered a follow up appointment with the Consultant.

Cutaneous complications associated with continuous subcutaneous infusions are common, ranging from mild nodule formation to painful hard nodules and in rare instances skin ulceration. It is important to minimise the development of nodules as it is thought that they may reduce the absorption of Apomorphine, thus reducing the efficacy of the treatment.

How to reduce nodule formation:
A 'clean' technique to administer the drug is essential to minimise local reactions, following initiation of Apomorphine therapy. It is important that patients and those who care for them are taught the correct administration technique.

- Rotate the injection site daily.
- On removing the needle, it is important to squeeze out any excess solution from the site and then massage the area with sudocrem, E45 cream or with ice cubes for a few minutes. This may help to reduce nodule formation.
- Silicone gel patches can also help to reduce nodule formation and relieve itchiness. The patches are placed over the nodules and left in place over night (or for up to 12 hours). The patches can be used many times if they are rinsed in warm water and dried carefully. Each packet of silicone gel contains instructions for use. (It is not fully understood how these patches work to reduce nodule formation).
- There have been some anecdotal reports that therapeutic ultrasound may be used with benefit on Apomorphine nodules. Some patients have received ultrasound treatment for many years and continue to maintain good skin quality and reduction in nodules. However, ultrasound therapy has not been subject to any formal trials. There is no clinical evidence to support its use or conversely to suggest that it is harmful, and it is rarely available in the community.
- Battery operated massagers available from some chemists can help reduces nodules.

Roles and responsibilities

Post/Group	Details
Care of the elderly consultants **Neurology consultants**	• Identification of patients potentially suitable for Apomorphine and onward referral of these patients to the Parkinson's Disease Specialist Practitioner for further assessment • Review ECG/Bloods/drug interactions and ensure no contraindications. • Refer patients to appropriate PDSP/Apomorphine nurse • Identify patients who would benefit from home initiation of Apo-morphine pump. • Withdrawal of treatment when no longer clinically appropriate
Parkinson's Disease Specialist Practitioner/Apo-morphine nurse	• Ongoing monitoring of effectiveness of treatment, side effects and prescribing via home care delivery scheme as per Trust guidelines • Appropriately timed appointments, alternating between Parkinson's Lead Consultant and PDSP (unless otherwise stated). • For patients attending for an Apomorphine challenge, request a challenge pack from Britannia/Dacepton to be delivered to pharmacy at Gloucestershire Royal Hospital. • For a continuous Apomorphine infusion, request an infusion pump from Britannia/Dacepton and accept delivery when arrives. • Organise and administer Apo-morphine challenge/initiate pump. • Offer patients and carers advice and support before, during after commencing Apo-morphine. • Prompt written documentation of the Apo-morphine challenge/pump initiation to be sent to the Specialist Consultant, GP, and patients.
COTE/Neurology Secretarial team	• Generation of prescriptions for home care delivery scheme to be signed by the Parkinson's Specialist Team ensuring that the patient has been reviewed in out-patients by a member of the team within the past 3 months and that bloods as above have been completed (for patients on continuous infusion only)

Contacts

Dr Sangeeta Kulkarni

Dr Mark Silva

Dr Peter Fletcher

PD Team

Israr Baig

Idris Bobat

Britannia: Britannia pump technical support Helpline which is 24 hours a day is Freephone 0808 1964242.

- Pharmacy order line 9am to 5pm 0844 880 1326
- Customer services email: customerservices@britannia-pharm.com
- Britannia nurse support email nursesupport@britannia-pharm.com

Ever Pharma-Nurses: Shelley Turner D-mine nurse Supervisor – Tel: 07889 540968 Email:shelley.turner2@nhs.net
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Ever Pharma Technical helpline 0800 254 0175 Ever Pharma medical information 0800 254 0174 (both are free phone numbers)
D-mine website for further information: www.d-minecare.co.uk

Costs

BNF 2020

APO-go pen 10mg/mL 3mL	£123.91 / 5 pens
APO-go prefilled syringe 5mg/mL 10mL	£73.11 / 5 pens
Dacepton 10mg/ml 3mL cartridge	£123.00 / 5 carts
Dacepton 100mg/20mL solution for infusion	£145 / 5 vials
Neria 60cm tubing 8mm/29g	£47.64 for 10
Neria 60cm tubing 10mm/29g	£47.64 for 10
NeriaGuard 60cm tubing 9mm/27g	£69.00 for 10
D-mine pump reservoir	£70 for 10
D-mine pen (replacement)	£100 per device

References

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

(2) National Institute for Health and Care Excellence. Parkinson's disease in adults: diagnosis and management. 2017

(3) Summary of product characteristics for APO-go PEN 10 mg/ml Solution for Injection. Last Updated on eMC 01/2020 accessed via https://www.medicines.org.uk/emc/product/2232/smpc

(4) Summary of product characteristics for APO-go pre-filled syringe. Last updated on eMC 02/2018 accessed via https://www.medicines.org.uk/emc/product/3908/smpc

(5) Summary of product characteristics for Dacepton 10 mg/ml solution for injection in cartridge. Last updated on eMC 19/11/2018 accessed via https://www.medicines.org.uk/emc/product/9650/smpc

(6) Summary of product characteristics for Dacepton solution for infusion. Last updated on eMC on 03/2017 accessed via https://www.medicines.org.uk/emc/product/9632/smpc

(7) Drug Tariff February 2020