Working in Partnership

SHARED CARE PRESCRIBING GUIDELINE

Apomorphine in Parkinson's disease

General Shared Care Guideline (SCG) Principles

- Medicines considered suitable for shared care are those which should be initiated by a Specialist, but where prescribing and monitoring responsibility may be transferred to Primary Care. Due to their potential side effects, shared care medicines usually require significant regular monitoring, and regular review by the Specialist is needed to determine whether the medicines should be continued. The best interest, agreement and preferences of the patient should be at the centre of any shared care agreement.

- The transfer of prescribing responsibility from the Specialist to the patient's General Practitioner (GP) or Primary Care prescriber should occur when both parties are in agreement that the patient's condition is stable or predictable, and that the Primary Care prescriber has the relevant knowledge, skills and access to equipment to allow them to monitor treatment as indicated in this shared care prescribing guideline.

- The aim of this guideline is to equip Primary Care prescribers with the information to confidently take on clinical and legal responsibility for prescribing the medication under a shared care agreement within their own level of competence.

- Within the Bedfordshire, Luton and Milton Keynes (BLMK) Integrated Care System (ICS), shared care guidelines are produced and updated through a robust governance process, following consultation with a wide range of key stakeholders. On this basis for BLMK ICS approved shared care guidelines, it is anticipated that Primary Care prescribers, upon individual assessment, will accept shared care for the patient if they felt it was clinically appropriate to do so and seek patient consent.

- If the Primary Care prescriber feels that a request for shared care cannot be accepted, i.e. falls outside of their own level of competence, they should initially seek further information or advice from the clinician who is sharing care responsibilities or from another experienced colleague in line with the General Medical Council (GMC) guidance.

- If the Primary Care prescriber is still not satisfied clinically to accept shared care, they should make appropriate arrangements for the patient's continuing care where possible. This may include asking another colleague in their practice to undertake the shared care. In the event that other colleagues in the practice also decline to share care, the Primary Care prescriber could seek assistance and advice from their Primary Care Network (PCN) (e.g. PCN Pharmacist).

- If the decision, after discussion with the PCN, is to decline shared care, the Primary Care prescriber must notify the Specialist clinician of their decision and reason (See appendix 1) to decline as soon as they can and in a timely manner (within a maximum of 14 to 21 days upon receipt of request) in writing and ensure the patient is aware of the change. In this scenario, the prescribing responsibility for the patient remains entirely with the Specialist. This principle also applies where shared care needs to be terminated in primary care e.g. due to lack of patient engagement. It is anticipated that these would be very rare events.

- The requirement for the Primary Care prescriber to send confirmation in writing via letter or approved electronic communication to the Specialist team for acceptance of shared care is NOT mandated.

- Where the hospital or Specialist clinician retains responsibility for monitoring drug therapy and/or making dosage adjustments, the Primary Care prescriber must be informed of any dose changes made as soon as possible to avoid medication errors. Similarly, if the Primary Care prescriber makes changes to the patient's medication regimen, the Primary Care prescriber must inform the Specialist in a timely manner. Primary Care prescribers can contact the Specialist team for advice, training and support as required.

- An agreed method of communication of blood test results and results of investigations between the Specialist, the Primary Care prescriber, the Community Pharmacist and the patient should be agreed at the onset of shared care and documented in the patient's notes in both Secondary care and Primary Care. Blood test results can usually be accessed electronically by both Secondary Care and Primary Care prescribers in the majority of cases. For some medications and in certain cases, the patient may elect to have a patient-held monitoring booklet, e.g. those on warfarin and lithium therapy.

- The principles above apply to shared care arrangements that involve the Specialist service sharing care with GPs and/or other Primary Care prescribers, e.g. Community Nursing Services. Where patient care is transferred from one Specialist service or GP practice to another, a new shared care agreement request must be commenced.

Document Control and History – Version Number: 2.0			
Original Author's Name & Job Title:	Samina Hassanali, Formulary and Medicines Safety Pharmacist		
Approval group:	BLMK Area Prescribing Committee	**Date of approval:**	4/12/24
Review Author's Name & Job Title:		**Date of last review:**	
Approval group:	BLMK Area Prescribing Committee	**Date of approval:**	4/12/24
Date of Next Review: (Unless clinical evidence changes)	December 2027		

Apomorphine in Parkinson's disease

Introduction and Aims of Shared Care:

Apomorphine is a potent dopamine-receptor agonist that is sometimes helpful in advanced disease for patients experiencing unpredictable 'off' periods with levodopa treatment. Apomorphine cannot be given orally because it undergoes extensive first pass metabolism to an inactive metabolite. It is usually given by intermittent subcutaneous (SC) injection or continuous SC infusion.

NICE NG71 makes the following recommendation for the use of apomorphine: 'Offer people with advanced Parkinson's disease best medical therapy, which may include intermittent apomorphine injection and/or continuous subcutaneous apomorphine infusion'.

This guideline highlights relevant prescribing issues with apomorphine and should be used in conjunction with relevant NICE guidance (NG71), the BNF, the Summary of Product Characteristics (SPC) and does not replace them. In practice, it is anticipated that there will only be a handful of patients across the whole BLMK area that can be successfully treated with Apomorphine.

1. AREAS OF RESPONSIBILITY

Secondary/Tertiary Care Prescribers or Specialist Team

Considerations prior to commencing apomorphine treatment:

- The decision to initiate apomorphine will be undertaken by a Specialist (primarily this will be a Consultant Neurologist although other specialists e.g., Care of the Elderly Consultants may initiate therapy (varies depending on geographical area).
- Apomorphine should only be recommended for use when the specialist/Parkinson's Disease Nurse Specialist (PDNS) is available to undertake the Apomorphine Challenge Trial and monitor treatment in the longer term.
- The intention to share care between the Specialist team (i.e., Specialist & PDNS) and the Primary Care Prescriber should be explained to the patient by a member of the specialist team. It is important that patients are consulted about treatment and agree with it.

- The Specialist should contact the patient's Primary Care Prescriber with a copy of the shared care arrangements BEFORE an apomorphine challenge test is carried out to ensure that they are willing to jointly manage the patient's therapy.
- Once agreement to share care has been received, the Specialist will then refer the patient to the Parkinson Disease Nurse Specialist (PDNS) (if involved – arrangements differ between areas) for consideration of an Apomorphine challenge trial.
- Ensure that all training, education, and professional support will be provided for all those involved by the PDNS/specialist.

Specialist responsibilities:

- To obtain patient informed consent for sharing of care between the Specialist, Primary Care prescriber and patient. Consenting parties must have sufficient, accurate, timely information in an understandable form. Consent must be given voluntarily and must be documented in the patient's notes.
- To confirm the working diagnosis.
- Assess the cautions, contraindications, and interactions.
- To confirm that the patient's condition has a predictable course of progression and the patient's care can be suitably maintained by Primary Care, following their medicine being optimised with satisfactory investigation results for at least 4 weeks.
- If shared care is considered appropriate for the patient, the patient's treatment regimen is confirmed, and benefit and safety of treatment is demonstrated via an apomorphine challenge trial, the Specialist will contact the Primary Care prescriber to initiate shared care.
- At the point of initial contact, the Specialist should check if the Primary Care prescriber can access blood test results electronically. If access is unavailable, the Specialist and the Primary Care prescriber should agree a process of communication to ensure blood test results and relevant results of investigations can be accessed by both parties in a timely manner.
- Following the request to the patient's Primary Care prescriber to initiate shared care; to ensure that the patient has an adequate supply of medication, ancillaries, consumables, and a sharps bin, until shared care arrangements are in place. Further prescriptions will be issued if, for unforeseen reasons, arrangements for shared care are not in place by the anticipated start date of the shared care (usually within 28 days or once the patient is stabilised on the medication). Patients should not be put in a position where they are unsure where to obtain supplies of their medication.
- To ensure that the Primary Care prescriber has sufficient information to enable them to monitor treatment, identify medicines interactions, and prescribe safely. This should include access or direction to a current copy of the SCG and contact details for the initiating Specialist. As a partner in the shared care agreement, the patient should, where appropriate, be provided with access or direction to a copy of the shared care guideline.
- The Specialist will provide the patient's Primary Care prescriber with the following information:
  - diagnosis of the patient's condition with the relevant clinical details
  - details of the patient's specialist treatment to date
  - details of treatments to be undertaken by the Primary Care prescriber (including reasons for choice of treatment, details of the dose, method of administration, the specific brand of apomorphine to prescribe, frequency of treatment, number of months of treatment to be given before review by the Specialist)
  - the type and number of infusion line/ needles (whichever is applicable), vials, cartridges and reservoirs associated with the specific apomorphine brand being used, sharps device (bin). See Appendix 2 for PIP codes for ancillaries for Dacepton®.
  - the date from which the Primary Care prescriber should prescribe the treatment.
  - details of other specialist treatments being received by the patient that are not included in shared care.
  - details of monitoring arrangements required.
- Whenever the Specialist sees the patient, he/she will:
  - send a written summary to the patient's Primary Care prescriber in a timely manner, noting details of any relevant blood test results or investigations if applicable.
  - confirm that ongoing treatment with the monitored medicine is appropriate.
  - record test results on the patient-held monitoring booklet if applicable and if this method of communication has been agreed at the onset of shared care.
  - confirm the current dosage and clearly highlight any changes made both to the patient and in writing to the patient's Primary Care prescriber who will action any of them as required.
- The Specialist team will:
  - provide training, advice, and guidance (as appropriate) for Primary Care prescribers if necessary to

support the shared care agreement.
  - initiate and continue the prescription of domperidone as required.
  - prescribe a sharps device (bin) and advise the patient on the local procedure for collection of sharps waste.
  - provide contact details for both working and non-working hours.
  - supply details for fast-track referral back to secondary/specialist care.
  - provide the patient with details of their treatment, follow-up appointments, monitoring requirements and, where appropriate, nurse specialist contact details
  - provide continued support for the Primary Care prescriber and answer any questions they may have on the treatment and the condition for which the medicine is being used.
- Prior to transfer of prescribing, the Specialist will:
  - Ensure that patients (and their caregivers, where appropriate) are aware of and understand their responsibilities to attend appointments and the need for continued monitoring arrangements.
  - Organise training for patient and carers to administer apomorphine if appropriate, including safe storage and disposal of sharps.
- The Specialist will document the decision to transfer prescribing of the treatment to the Primary Care prescriber via the shared care guideline in the patient's hospital medical notes. If the Primary Care prescriber declines the request for shared care and the Specialist is therefore responsible for the prescribing of the medication for the patient, the Specialist will document this in the patient's hospital medical notes.

All the above information should be provided to the Primary Care Prescriber in writing via a letter or approved electronic communication.

Primary Care Prescribers

- To prescribe within their own level of competence. The (GMC) guidance on "Good practice in prescribing and managing medicines and devices" states that doctors are responsible for the prescriptions they sign and their decisions and actions when they supply and administer medicines and devices or authorise or instruct others to do so. They must be prepared to explain and justify their decisions and actions when prescribing, administering, and managing medicines.
- The same principles apply to non-medical prescribers as well as medical prescribers as outlined in the "Competency Framework for all Prescribers".
- To confirm that the patient or carer consents to sharing of care between the Specialist, Primary Care prescriber and patient. Consenting parties must have sufficient, accurate, timely information in an understandable form. Consent must be given voluntarily and must be documented in the patient's notes.
- If shared care is accepted, commencement of shared care must be clearly documented in the patient's Primary Care medical notes.
- If declining the request for shared care, the decision and rationale should be explained to the Specialist in writing as soon as is possible and in a timely manner, within a maximum of 14 to 21 days upon receipt of request. The patient should also be informed of the decision.
- Ensure that he/she has the information and knowledge to understand the therapeutic issues relating to the patient's clinical condition.
- Undergo any additional training necessary to carry out the prescribing and monitoring. The specialist can provide education and training.
- Agree that in his/her opinion the patient should receive shared care for the diagnosed condition unless good reasons exist for the management to remain within Secondary/Specialist care.
- Prescribe the specific apomorphine brand in accordance with the written instructions contained within the SCG or other written information provided and communicate any changes of dosage made in Primary Care to the patient. Prescribe apomorphine at the dose and for the route of administration recommended by the specialist team and prescribe the relevant needles / infusion lines / sharps device (bin) (See Appendix 2 for details). It is the responsibility of the prescriber making a dose change to communicate this to the patient.
- Report any adverse effect in the treatment of the patient to the Specialist team, and via the MHRA Yellow Card Scheme https://yellowcard.mhra.gov.uk/.
- The Primary Care prescriber will ensure that the patient is monitored as outlined in the SCG and will take the advice of the referring Specialist if there are any amendments to the suggested monitoring schedule.
- If patient is prescribed apomorphine in combination with domperidone, check the QT interval if clinically indicated, (e.g., if a QT-prolonging or interacting medicine is started or if symptoms of cardiac side effects are reported) and advise patients to inform their doctor (Specialist or GP) / Specialist Nurse of any changes that could increase their risk of arrhythmia).)

- The Primary Care prescriber will ensure a robust monitoring system is in place to ensure that the patient attends the appropriate appointments in Primary Care for follow-up and monitoring, and that defaulters from follow-up are contacted to arrange alternative appointments. It is the Primary Care prescriber's responsibility to decide whether to continue treatment for a patient who does not attend appointments required for follow-up and monitoring, and to inform the Specialist of any action taken.
- Primary Care prescribers are not expected to be asked to participate in a shared care arrangement where:
    - a locally approved SCG doesn't exist, or the medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care agreement.
    - the prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care.
- Where community nurse involvement is required in the administration of medicines under a SCG, nurses should be provided with adequate information, education, training and guidance by the prescriber or the Specialist. Arrangements should be made in good time for any potential problems to be resolved to ensure that patient care is not compromised.

Patient and/or carer

- To provide their informed consent for sharing of their care with the Specialist and Primary Care prescriber. Consenting parties must have sufficient, accurate, timely information in an understandable and accessible format. Consent must be given voluntarily and must be documented in the patient's notes. Supporting information is available from NICE "Making decisions about your care".
- To take their medication as agreed, unless otherwise instructed by an appropriate healthcare professional.
- To meet all necessary monitoring arrangements to ensure the safe prescribing of their medication, and to alert the prescriber where these arrangements are not met.
- To attend all follow-up appointments with the Primary Care prescriber and Specialist. If the patient is unable to attend any appointments, they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.
- Inform healthcare professionals of their current medications prior to receiving any new prescribed or over-the-counter medication. It is also important that the specialist and Primary Care prescriber are made aware of any other medications that the patient is taking which may not appear in the patient's medical records, such as OTC products, any medicinal products obtained privately, any recreational drugs, herbal medicines, etc.
- Report the use of any new prescribed or over the counter medications to their primary care prescriber.
- Reporting of all suspected adverse reactions to medicines to their Primary Care prescriber.
- Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines.
- If wishing to self-administer, agree to appropriate training and to protocols for the safe disposal of sharps.
- Store their medication securely away from children and according to the medication instructions.
- Read the information supplied by their Primary Care prescriber, Specialist and Pharmacist and contact the relevant practitioner if they do not understand any of the information given.
- An agreed method of communication of results of investigations between the Specialist, the Primary Care prescriber, the Community Pharmacist and the patient should be agreed at the onset of therapy.

Community Pharmacist

- Know where to access locally agreed shared care guidelines to aid professional clinical check of prescription prior to dispensing.
- Professionally check prescriptions to ensure they are safe for the patient and contact the Primary Care prescriber if necessary to clarify their intentions.
- A method of communication of results of investigations between the Specialist, the Primary Care prescriber, the Community Pharmacist and the patient should be agreed at the onset of therapy.
- Fulfil legal prescriptions for medication for the patient unless they are considered unsafe.
- Counsel the patient on the proper use of their medication.
- Advise patients suspected of experiencing an adverse reaction to their medicines to contact their Primary Care prescriber or Specialist/Specialist nurse team.

2. COMMUNICATION AND SUPPORT

Hospital / Specialist contact information *(The referral letter will indicate named consultant)*	**Out-of-hours contact details & procedures:**
Hospital name and address: Bedfordshire Hospital Foundation Trust **Consultant names:** Dr Amit Batla **Role and specialty**: Movement Disorder Specialist Neurologist **Tel number:** 01582 718240 **Email address:** Amit.Batla@bedsft.nhs.uk **Hospital name and address:** Cambridgeshire University Hospitals **Consultant names:** Dr Paul Worth. **Role and specialty:** Consultant Neurologist **Email address:** paulworth1@nhs.net **Alternative contact (e.g. for clinic or specialist nurse):** PDNS (ELFT Community Services, Bedfordshire) Hazel White (ELFT Community Services, Bedfordshire) 01234 310118 hazel.white7@nhs.net Parkinson's Nurse Service via Single point of Access 9-5pm 0345 6024064.	**EVER Pharma (Dacepton)** Technical support for patients, families and carers to assist with device related issues. **0800 254 0175** Monday–Sunday: 07:00– 22:00 ever.pharma@nhs.net
Hospital name and address: Luton & Dunstable Hospital Specialists **Consultant names:** Dr Amit Batla **Role and specialty**: Movement Disorder Specialist Neurologist **Tel number:** 01582 718240 **Email address:** Amit.Batla@bedsft.nhs.uk **Consultant names:** Dr Paul Watts **Role and specialty:** Consultant Neurologist **Tel number:** 01582 718240	**EVER Pharma (Dacepton)** Technical support for patients, families and carers to assist with device related issues. **0800 254 0175** Monday–Sunday: 07:00– 22:00 ever.pharma@nhs.net

Email address: paul.watts@ldh.nhs.uk **Consultant names**: Dr Anna Latorre **Role and specialty**: Movement Disorder Specialist Neurologist **Tel number:** 01582 718240 **Email address:** Anna.Latorre@bedsft.nhs.uk **Consultant names:** Dr Susantha Nawaratne-Wijayasiri **Role and specialty**: Geriatrician, PD Specialist Lead **Tel number:** 01582 497504 **Email address**: Susantha.Wijayasiri@bedsft.nhs.uk **Alternative contact** (e.g. for clinic or specialist nurse): **Neurology Specialist Nurse** Karina Lucas 01582 491166 ext. 3182 Karina.Lucas@bedsft.nhs.uk Aneta Simeonova aneta.simeonova@nhs.net	
Hospital name and address: Milton Keynes Hospital Specialists **Consultant names:** Dr John Jacob **Role and specialty:** Consultant Neurologist **Tel number**: 01908 997070 **Email address:** john.jacob@mkuh.nhs.uk **Alternative contact** (e.g., for clinic or specialist nurse): Ania Pearson ania.pearson@nhs.net 01908 724554	Contact Hospital A&E: 01908 660033
Specialist support / resources available to Primary Care prescriber including patient information:	

Pharmacy Department: Principal Medicines Information Pharmacist

Bedford Hospital
Medication Helpline
01234 792175
Monday – Friday, 8.30am – 4.30pm
bhn-tr.medicinesinformation.formulary@nhs.net

Luton & Dunstable Hospital
Medicine Information Pharmacist
01582 497114 / 01582 497367
Monday to Friday 10am-2pm
drug.info@ldh.nhs.uk

Milton Keynes Hospital
Pharmacy Medicines Information
01908 995738
information.medicines@mkuh.nhs.uk

Britannia Pharmaceuticals
(APO-go)
APO-go helpline
0118 9209500
www.apo-go.co.uk

EVER Pharma (Dacepton)

Technical support for patients, families and carers to assist with device related issues.
0800 254 0175
Monday–Sunday: 07:00– 22:00
ever.pharma@nhs.net

For patient support relating to prescriptions and ordering
0800 254 0176
Monday–Friday: 08:00–16:00
info.uk@everpharma.com

HCPs are able to contact the D-mine® Care Nurse Advisors directly for support.
Monday–Friday: 09:00–17:30

Prescription and Ordering Support for NHS Trusts 0800 254 0176
Monday–Friday: 08:00–16:00 or email info.uk@everpharma.com

Parkinson's UK Patient Information on Apomorphine
https://www.parkinsons.org.uk/information-and-support/apomorphine
Parkinson's UK National Helpline – 0808 800 0303

3. CLINICAL INFORMATION

Indication(s): **(Please state whether licensed or unlicensed)**	Parkinson's Disease (licensed): Treatment of motor fluctuations ("on-off" phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication.
Place in therapy:	In patients not sufficiently controlled by oral anti-Parkinson medication.
Therapeutic summary:	Apomorphine is a potent dopamine-receptor agonist that is sometimes helpful in advanced disease for patients experiencing unpredictable 'off' periods with

	levodopa treatment
Initiation and ongoing dose regime and Route of administration: *(See Summary of Product Characteristics (SPC) for full list)*	*Note: Transfer of monitoring and prescribing to Primary Care is normally after the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.* **Initial stabilisation:** *(The loading period must be prescribed by the initiating Specialist)* Apomorphine response test: Start domperidone 10mg three times daily at least two days prior to apomorphine therapy and arrange apomorphine response test. The appropriate dose for each patient is established by incremental dosing schedules. The following schedule is suggested: *Intermittent subcutaneous injection* 1 mg of apomorphine hydrochloride hemihydrate (0.1 ml), 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 hydrochloride hemihydrate (0.2 ml) 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. **Maintenance dose (following initial stabilisation):** (*The initial maintenance dose must be prescribed by the initiating Specialist)* The daily dose of apomorphine varies widely between patients, typically within the range of 3-30 mg, 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 100 mg and that individual bolus injections should not exceed 10 mg. The initial maintenance dose must be prescribed by the initiating specialist. Once apomorphine treatment is established, the domperidone dose can be gradually reduced and then discontinued by the specialists. **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

<table>
<tr><td></td><td colspan="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.

This schedule must be prescribed by the initiating specialist.

<u>Conditions requiring dose adjustment</u>:
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.</td></tr>
<tr><td>Duration of treatment:</td><td colspan="4">When treatment is considered to be no longer efficacious or if side effects outweigh benefit - treatment is to be discontinued</td></tr>
<tr><td>Preparations available (Manufacturer):</td><td colspan="4">APO-go (ampoule, pen, and pre-filled syringe) and Dacepton (vial and cartridge)</td></tr>
<tr><td rowspan="6">Summary of adverse effects:
(See Summary of Product Characteristics (SPC) for full list)

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme.</td><td colspan="2">Adverse effect</td><td>Frequency/ likelihood</td><td>Management</td></tr>
<tr><td rowspan="2">Blood and lymphatic system disorders</td><td>Haemolytic anaemia and thrombocytopenia</td><td>Uncommon</td><td rowspan="2">Urgent referral to initiating specialist if discovered.</td></tr>
<tr><td>Eosinophilia</td><td>Rare</td></tr>
<tr><td>Immune system disorders</td><td>Due to the presence of sodium metabisulphite, allergic reactions (including anaphylaxis and bronchospasm) may occur</td><td>Rare</td><td>Emergency referral to hospital.</td></tr>
<tr><td rowspan="2">Psychiatric disorders</td><td>Hallucinations</td><td>Very common</td><td rowspan="2">Seek advice from specialist.</td></tr>
<tr><td>Neuropsychiatric disturbances (including transient mild confusion and visual hallucinations).</td><td>Common</td></tr>
</table>

		Impulse control disorders: Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating, and compulsive eating can occur in patients treated with dopamine agonists including apomorphine. Aggression, agitation.	*Not known*	Patients should be regularly monitored for the development of impulse control disorders. Refer to specialist as dose reduction/tapered discontinuation should be considered if such symptoms develop.
		Dopamine dysregulation Syndrome (DDS)	An addictive disorder resulting in excessive use of the product seen in some patients treated with apomorphine.	Refer to specialist.
	Nervous system disorders	Transient sedation with each dose of apomorphine HCl at the start of therapy may occur; this usually resolves over the first few weeks.	*Common*	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 may be considered. Refer to the specialist.
		Apomorphine is associated with somnolence. Dizziness / light-headedness have also been reported.		
		Apomorphine may induce dyskinesias during 'on' periods, which can be severe in some cases, and in a few patients may result in cessation of therapy. Apomorphine has been associated with sudden sleep onset episodes.	*Uncommon*	
		Syncope Headache	*Not known*	

	Vascular disorders	Postural hypotension is seen infrequently and is usually transient.	*Uncommon*	Seek advice from specialist if not transient.
	Respiratory, thoracic, and mediastinal disorders	Yawning has been reported during apomorphine therapy.	*Common*	
		Breathing difficulties have been reported.	*Uncommon*	Seek advice from specialist
	GI disturbance:	Nausea, vomiting.	*Common*	Particularly when apomorphine treatment is first initiated, usually because of the omission of domperidone.
	Skin and subcutaneous tissue disorders	Local and generalised rashes have been reported.	*Uncommon*	
	General disorders and administration site conditions	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.	*Very common*	These can sometimes be reduced by the rotation of injection sites or possibly using ultrasound (if available) to avoid areas of nodularity and induration. Seek advice from the specialist.
		Injection site necrosis and ulceration have been reported.	*Uncommon*	
		Peripheral oedema has been reported.	*Not known*	
	Investigations	Positive Coombs' tests have been reported for patients receiving apomorphine.	*Uncommon*	
Monitoring requirements by Specialist (baseline investigations, initial monitoring and ongoing monitoring):	**<u>Baseline investigations</u>:** • Full blood count (FBC) • Reticulocyte count • Coombs' test			

<table>
<tr><td></td><td colspan="4">

Liver function tests (LFTs)
Renal function tests (U&Es)
ESR
Blood Pressure and cardiovascular function
QT-interval before starting domperidone.

<u>Initial monitoring</u>: (Monitoring at baseline and during initiation is the responsibility of the Specialist until the patient is optimised and stabilised on the medicine with no anticipated further changes)
Monitoring to be conducted at 1 month ·
• Lying and standing blood pressure
• FBC
• Reticulocyte count
• QT-interval during the apomorphine initiation phase

<u>Ongoing monitoring (at 6-12 monthly intervals)</u>:

FBC
Renal function test (U&Es)
Liver function test (LFTs)
Check the QT-interval if clinically indicated (e.g., if a QT-prolonging or interacting drug is started or if symptoms of cardiac side effects are reported)

</td></tr>
<tr><td rowspan="2">Ongoing monitoring requirements by Primary Care prescriber (if specialists have not completed):</td><td>Monitoring</td><td>Frequency</td><td>Result</td><td>Action for Primary Care prescriber</td></tr>
<tr><td>

FBC
Renal function test (U&Es)
Liver function test (LFTs)
Check the QT-interval if clinically indicated (e.g., if a QT-prolonging or interacting drug is started or if symptoms of cardiac side effects are reported)

</td><td>Every 6-12 months.</td><td>
If significant electrolyte disturbance, QT interval should be assessed via ECG.

if WBC < 4x109 /L or neutrophils < 2 x 109 /L or platelets < 150x109 /L
if creatinine > 150 µmol/L
if potassium > 5.5 mmol/L
if ALT >62 IU/L in women or > 80 IU/L in men

</td><td>Consult promptly with the specialist team if the patient deteriorates, has problems administering apomorphine, or when test results are abnormal (Primary Care Prescriber may continue treatment while seeking advice), or if patient defaults from blood test appointments.

Urgent referral to initiating specialist if prolonged QT- interval is discovered.</td></tr>
</table>

Clinically relevant drug interactions and advice on management: *Note: This does not replace the SPC and should be read in conjunction with it.*	Drug interaction	Management / Action for Primary Care prescriber
(See Summary of Product Characteristics (SPC) for full list)	• Patients selected for treatment with apomorphine HCl are almost certain to be taking concomitant medications for their Parkinson's disease. In the initial stages of apomorphine HCl therapy the patient should be monitored for unusual side-effects or signs of potentiation of effect. • Neuroleptic medicinal products may have an antagonistic effect if used with apomorphine. There is a potential interaction between clozapine and apomorphine, however clozapine may also be used to reduce the symptoms of neuropsychiatric complications. • If neuroleptic medicinal products have to be used in patients with Parkinson's disease treated by dopamine agonists, a gradual reduction in apomorphine dose may be considered when administration is by minipump or syringe-driver (symptoms suggestive of neuroleptic malignant syndrome have been reported rarely with abrupt withdrawal of dopaminergic therapy). • Concomitant use of apomorphine with ondansetron may lead to severe hypotension and loss of consciousness and is therefore contraindicated. Such effects might also occur with other 5-HT3 antagonists. **Antihypertensive and Cardiac Active Medicinal Products** • Even when co-administered with domperidone,	Seek advice from specialist.

	apomorphine may potentiate the antihypertensive effects of these medicinal products. • It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval. Consult: http://www.sads.org.uk/drugs-to-avoid/ for up-to-date guidance.	Urgent referral to initiating specialist if prolonged QT- interval is discovered.
Clinically relevant precautions and contraindications: ***Note: This does not replace the SPC and should be read in conjunction with it.***	**<u>Cautions/Precautions</u>:** • Apomorphine 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 antihypertensives, and especially in patients with pre-existing postural hypotension. • Since apomorphine, especially at high doses, may have the potential for QT prolongation, caution should be exercised when treating patients at risk for torsades de pointes arrhythmia. • When used in combination with domperidone, risk factors in the individual patient should be carefully assessed. This should be done before treatment initiation, and during treatment. Important risk factors include serious underlying heart conditions such as congestive cardiac failure, severe hepatic impairment, or significant electrolyte disturbance. Also, medication possibly affecting electrolyte balance, CYP3A4 metabolism or QT interval should be assessed. Monitoring for an effect on the QTc interval is advisable. An ECG should be performed: - prior to treatment with domperidone - during the treatment initiation phase - as clinically indicated thereafter. • The patient should be instructed to report possible cardiac symptoms including palpitations, syncope, or near-syncope. They should also report clinical changes that could lead to hypokalaemia, such as gastroenteritis or the initiation of diuretic therapy. • At each medical visit, risk factors should be revisited. • Apomorphine is associated with local subcutaneous effects. These can sometimes be reduced by the rotation and massage of injection sites and good skin hygiene. • Haemolytic anaemia and thrombocytopenia have been reported in patients treated with apomorphine. Haematology tests, as recommended with levodopa, should be undertaken at regular intervals. • 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 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.
	• Note recent MHRA warnings on the use of domperidone:
	  ○ Drug Safety Update December 2019
	  ○ Drug Safety Update April 2016
	  ○ Drug Safety Update May 2014
	• Dopamine Dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of the product seen in some patients treated with apomorphine. Before initiation of treatment, patients and caregivers should be warned of the potential risk of developing DDS.
	• APO-go® and Dacepton® contains sodium metabisulfite which may rarely cause severe hypersensitivity reactions and bronchospasm.
	
	Contraindications:
	• Hypersensitivity to the active substance or to any of the excipients.
	• Patients with respiratory depression, dementia, psychotic diseases or hepatic insufficiency.
	• Patients who have an "on" response to levodopa which is marred by severe dyskinesia or dystonia.
	• The concomitant use of apomorphine with ondansetron is contraindicated (see interactions).
	• Children and adolescents under 18 years of age
	• Domperidone should NOT BE USED in patients with serious underlying heart conditions. Domperidone should be avoided in patients who are taking concomitant medication known to cause QT prolongation (such as ketoconazole and erythromycin)
	
	Please see SPC for comprehensive information.

Renal impairment:	Apomorphine HCl should be given with caution to patients with renal disease. In renal impairment extra caution is recommended during initiation of therapy in patients because of the risk of postural hypotension.
Hepatic impairment:	Contraindicated in patients with hepatic insufficiency. When used in combination with domperidone, risk factors in the individual patient should be carefully assessed. Important risk factors include severe hepatic impairment. Monitoring for an effect on the QTc interval is advisable. An ECG should be performed
Advice to patients and carers: *The Specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.*	The patient should be advised to report any of the following signs or symptoms to their Primary Care prescriber without delay: • possible cardiac symptoms including palpitations, syncope, or near-syncope. They should also report clinical changes that could lead to hypokalaemia, such as: • gastroenteritis • or the initiation of diuretic therapy. Apomorphine has been associated with somnolence and episodes of sudden sleep onset:

	• 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. 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. Dopamine Dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of the product seen in some patients treated with apomorphine. Before initiation of treatment, patients and caregivers should be warned of the potential risk of developing DDS.
Pregnancy, paternal exposure and breastfeeding: *It is the Specialist's responsibility to provide advice on the need for contraception to male and female patients where applicable on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the Primary Care prescriber and the Specialist.*	**Pregnancy:** There is no experience of apomorphine usage in pregnant women. Animal reproduction studies do not indicate any teratogenic effects, but doses given to rats which are toxic to the mother can lead to failure to breathe in the newborn. The potential risk for humans is unknown. Apomorphine should not be used during pregnancy unless clearly necessary. **Breastfeeding:** It is not known whether apomorphine is excreted in breast milk. A decision on whether to continue/discontinue breastfeeding or to continue/discontinue therapy should be made taking into account the benefit of breast-feeding to the child and the benefit to the woman.
Practical issues and supply of ancillary equipment (where relevant):	**Supply of ancillary equipment** The specialist will list the drugs, ancillaries, and consumables to be prescribed in primary care in the referral letter. The required number of needles / infusions lines (whichever is applicable), sharps device (bin) should also be prescribed to cover at least the first 28 days treatment. **If prescribing APO-go® product:** • Apomorphine pre-filled syringes (APO-go pens and APO-go PFS) (Insupen needles for pens are provided by Britannia) • Infusion lines (when apomorphine is used as an infusion) – see drug tariff for available options. • Sharps bin • Tegaderm dressings **Sharps device (bins)** - The PDNS/specialist should issue the first sharps device (bin) and advise the patient on the correct disposal process (This may vary between different geographical areas). **The following are NOT available on FP10 but may be obtained as follows**: • APO-go ambulatory infusion pumps are available on loan from Britannia via the PDNS/specialist. • Crono-APO-go syringes for use in an APO-go ambulatory infusion pump can be obtained by the Community Pharmacist directly from

	Britannia pharmaceuticals. **<u>If prescribing Dacepton® product:</u>** • Contact the Bionical nurses for specific advice as this varies between patients
	<u>Practical issues / Pharmaceutical precautions</u> **APO-go Pens and APO-go PFS:** • Should be stored below 25°C in the original outer cartons to protect from light. • Do not use if the solution has turned green. • Once in use, APO-go pens have a 48h expiry. The below items are available to order via Alliance Healthcare only: **Dacepton 30mg/3ml sol for injection cartridges:** • Should be stored below 25°C in the original outer carton to protect from light. • The product should be stored at the same conditions after opening and between withdrawals. • Do not refrigerate or freeze. • Do not use if the solution has turned green. • The solution should be inspected visually prior to use. Only clear, colourless to slightly yellow solutions free of particles in undamaged containers should be used. • After first opening: chemical and physical in-use stability has been demonstrated for 15 days at 25°C. • Discard each cartridge with any unused content not later than 15 days after first opening. • From a microbiological point of view, unless the method of opening and further handling precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. **Dacepton 100mg/20ml solution for infusion:** • Should be stored below 25°C in the original outer carton to protect from light. • The product should be stored at the same conditions after opening and between withdrawals. • Do not refrigerate or freeze. • Do not use if the solution has turned green. • The solution should be inspected visually prior to use. Only clear and colourless to slightly yellow solutions without particles, in undamaged containers, should be used. • For single use only. Any unused medicinal product or waste material should be disposed in accordance with local requirements. • After opening and filling the drug product in syringes attached with infusion sets: chemical and physical in-use stability has been demonstrated for 7 days at 25°C. From a microbiological point of view, unless the method of opening and further handling precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.
Key references:	• eBNF accessed via BNF (British National Formulary) | NICE on

04/04/2024

- APO-go AMPOULES 10mg/ml Solution for Injection or Infusion. Britannia Pharmaceuticals Limited. Date of revision of the text: 22 February 2018. Accessed via Home - electronic medicines compendium (emc) on 04/04/2024.
- APO-go Pen 10mg/ml Solution for Injection. Britannia Pharmaceuticals Limited. Date of revision of the text: 02/2022. via Home - electronic medicines compendium (emc) on 04/04/2024.
- APO-go PFS 5mg/ml Solution for Infusion in Pre-filled Syringe. Britannia Pharmaceuticals Limited. Date of revision of the text 22 February 2018: Accessed via Home - electronic medicines compendium (emc) on 04/04/2024.
- APO-go POD 5 mg/ml solution for infusion in cartridge. Britannia Pharmaceuticals Limited. Date of revision of the text: 23/5/2023. Accessed via Home - electronic medicines compendium (emc) on 04/04/2024.
- Dacepton 10 mg/ml solution for injection in cartridge. Ever Pharma UK Limited. Date of revision of the text: 30/11/2023. Accessed via Home - electronic medicines compendium (emc) on 04/04/2024.
- Dacepton 5 mg/ml solution for infusion. Ever Pharma UK Limited. Date of revision of the text: 30/11/2023. Accessed via Home - electronic medicines compendium (emc) on 04/04/2024.
- Domperidone 10mg Tablets. Aurobindo Pharma - Milpharm Ltd. Date of revision of the text: 08/04/2021. Accessed via Home - electronic medicines compendium (emc) on 04/04/2024.
- NICE. NG71: Parkinson's disease in adults. Published: 19 July 2017. Accessed via https://www.nice.org.uk/guidance/ng196 on 04/04/24.
- MHRA. Drug Safety Update: Apomorphine with domperidone: minimising risk of cardiac side effects. 11 December 2014. Accessed via Domperidone: risks of cardiac side effects - GOV.UK (www.gov.uk) on 05/04/24.
- MHRA. Drug Safety Update: Domperidone: risks of cardiac side effects. 18 April 2016. Accessed via Apomorphine with domperidone: minimising risk of cardiac side effects - GOV.UK (www.gov.uk) on 05/04/24

This shared care guideline is to be read in conjunction with the following document

- **NHSE/NHSCC guidance – items which should not be routinely prescribed in Primary Care: guidance for CCGs – link here**
- **NHSE policy – Responsibility for prescribing between Primary & Secondary/Tertiary Care – link here**

FLOWCHART DEMONSTRATING THE USE OF APOMORPHINE IN PARKINSON'S DISEASE SHARED CARE PROTOCOL involving a Parkinson's Disease Nurse Specialist

(Refer to Full Shared Care Guideline for full list of responsibilities and for more detailed information)

Specialist Responsibilities

- Confirm diagnosis, carry out baseline tests and check QT interval (if domperidone is to be prescribed) (see appendices 2&3 for ECG monitoring advice).
- Assess patient's clinical suitability for apomorphine.
- Check for any contraindications before requesting a challenge trial.
- Check for possible drug interactions when considering apomorphine therapy.
- Liaise with GP regarding shared care before a challenge test is considered.
- Liaise with PDNS regarding apomorphine challenge test and arrange for the patient to receive domperidone 2 days prior to the test.
- Provide information to patient and GP about apomorphine and the necessary monitoring requirements.

Parkinson's Disease Nurse Specialist (PDNS) Responsibilities

- Ensure the patient has received domperidone for 2 days prior to apomorphine challenge test. (Check QT interval - See appendices 3 and 4 of shared care guideline for details of dosing regimen and ECG monitoring advice, as recommended by Assoc. British Neurologists and MHRA)
- Conduct the "challenge test" and determine dose of apomorphine.
- Prescribe initial 28 days treatment, consisting of:
  - Apomorphine (continuous infusion or s/c pens, whichever is applicable)
  - Domperidone (off label use – see appendix 3 & 4) if applicable)
  - Additional needles /infusion lines / sharps bin
- Train patient/carer on how to use S/C injection/infusion devices.

Specialist / PDNS Further Responsibilities

- Review patient at regular intervals (minimum 3 monthly)
- Optimise patient's medication.
- Monitor and evaluate adverse drug reactions.
- Carry out ongoing monitoring of PD symptoms, drug response and blood pressure (and refer if applicable)
- Be a point of contact for community teams and patients and provide information and support to GPs, patient, and carers.
- Arrange training for District Nurse re: using apomorphine infusion pumps and syringes.
- Have mechanisms in place to rapidly refer deteriorating patients.
- Have mechanisms in place to deal with mechanical failure of apomorphine pump.

GP Responsibilities

- Agree to share care.
- Communicate with PDNS / Specialist
- Prescribe ongoing apomorphine, needles / infusion lines and any concomitant therapy.
- **Check QT interval if clinically indicated** if patient is prescribed apomorphine and domperidone (see Appendices 3 & 4)
- **Monitoring tests and bloods every 6-12 months.**

 Consult specialist team when appropriate (e.g. patient deteriorates,

Patient Responsibilities

- Attend for blood tests and reviews.
- Inform nurse/ doctor of any adverse effects and / or concerns.
- Report any suspected pregnancy (patient or partner)
- Collect repeat prescriptions.
- Dispose of sharps appropriately.

Communication: Specialist to GP

- **Invite** GP to share care;
- Communicate baseline test results and treatment plan
- Provide details of the type of monitoring tests needed and the monitoring intervals required.
- Provide back-up advice when required

Communication: GP to PDNS / Specialist

Contact the PDNS / Specialist if:

- Patient deteriorates
- Patient has problems administering apomorphine
- Abnormal test results
- Patient does not attend for blood test monitoring

In the case of an urgent query, the GP should contact the PDNS or the individual Trust's Neurology

Communication: PDNS to GP

- Provide information regarding:
  - apomorphine dose and route of administration
  - concomitant medication e.g. domperidone (if required)
  - details of additional items required e.g needles/ infusion lines
- Advise on monitoring requirements
- Inform GP of any dose changes
- Provide point of contact for GP and patient.

Individual Companies 24 hour Helpline for problems with pump or pens: - Apo-Go® Britannia 0808 1964242; **Dacepton®** D-mine® Care support line on 0800 254 0175

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust.

Appendix 1

Possible reasons for a Primary Care Prescriber to decline to accept shared care:

1	I do not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care. I have consulted with other Primary Care prescribers in my practice who support my decision. I have discussed my decision with the patient and request that prescribing for this individual remains with you due to the sound clinical basis given above.
2	The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement (medicine not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine).
3	The patient has not had the minimum duration of supply of medication to be provided by the initiating Specialist. Therefore, please contact the patient as soon as possible in order to provide them with the appropriate length of supply of the medication before transferring the prescribing responsibility to the Primary Care prescriber.
4	The patient has not been optimised/stabilised on this medication. Therefore, please contact the patient as soon as possible in order to provide them with the medication until the patient is optimised on this medication before transferring the prescribing responsibility to the Primary Care prescriber.
5	Shared Care Guideline and/or relevant clinical information as stipulated in the guideline not received. Therefore, please contact the patient as soon as possible in order to provide them with the medication until I receive the appropriate Shared Care Guideline before transferring the prescribing responsibility.
6	Other (Primary Care prescriber to complete if there are other reasons why shared care cannot be accepted or why shared care is to be discontinued if already started, e.g. adverse effects): ……

Appendix 2

Dacepton® PIP codes and ordering information.

The below items are available to order via Alliance Healthcare only:

Pump Therapy:

PIP	Product Description	Pack Size	Qty of Packs Required
4093878	Dacepton® 100mg/20ml sol for infusion vials	5	
4101234	D-mine® Pump Reservoir	10	
4231866	D-mine® Infset (subcutaneous Infusion Line 28g/8mm)	25	

Infusion lines
When ordering Dacepton® 100mg/20ml solution for infusion vials, please ensure the patient is also prescribed at least 30 infusion lines per month. The manufacturer **recommends D-mine® Infset for subcutaneous infusion with a needle diameter of 28G**. Infusion sets from other manufacturers can be used according to their stated compatibility details.

Pen Therapy:

PIP	Product Description	Pack Size	Qty of Packs Required
4093761	Dacepton® 30mg/3ml sol for injection cartridges	5	
*2393452	BD Micro-Fine Ultra Pen Needles 8mm (31g) x 100	1	

***Pen Needles**
When ordering Dacepton® 30mg/3ml solution for injection cartridges, please ensure the patient is also prescribed sufficient quantities of Pen Needles (packs of 100) per month prescription. The manufacturer recommends range of **BD™ pen needles 29-31 gauge** (diameter 0.25 – 0.33 mm) and 5 - 12.7 mm length. Pen needles from other manufacturers can be used according to their stated compatibility details.

Medical Devices – Available to order from EVER Pharma via quality.uk@everpharma.com

DESCRIPTION: MEDICAL DEVICES	PACK SIZE	QTY REQUIRED
D-mine® Pen Medical Device (for use with Dacepton® cartridge)	**1**	
D-mine® Pump Medical Device (for use with Dacepton® vials)	**1**	

Appendix 3

MHRA Drug Safety Updates

Apomorphine with domperidone: minimising risk of cardiac side effects

From: Medicines and Healthcare Products Regulatory Agency (MHRA)
Published: 18 April 2016

Patients receiving apomorphine and domperidone require an assessment of cardiac risk factors and ECG monitoring to reduce the risk of serious arrhythmia related to QT-prolongation.
1. Domperidone and the risk of cardiac side effects
2. Apomorphine with domperidone and the risk of QT-prolongation
3. Further information

Advice for healthcare professionals:

- Before starting treatment, carefully consider whether the benefits of concomitant apomorphine and domperidone treatment outweigh the small increased risk of cardiac side effects.
- Discuss the benefits and risks of apomorphine with patients and carers and advise them to contact their doctor immediately if they develop palpitations or syncopal symptoms during treatment.
- Check the QT-interval before starting domperidone, during the apomorphine initiation phase and if clinically indicated thereafter (e.g. if a QT-prolonging or interacting drug is started or if symptoms of cardiac side effects are reported)
- Regularly review domperidone treatment to ensure patients take the lowest effective dose for the shortest duration.
- Advise patients to inform their doctor of any changes that could increase their risk of arrhythmia, such as:
- symptoms of cardiac or hepatic disorders
- conditions that could cause electrolyte disturbances (eg, gastroenteritis or starting a diuretic)
- starting any other medicines
- Please continue to report suspected side effects to apomorphine, domperidone, or any other medicine on a Yellow Card

Apomorphine (brand names: APO-go, Dacepton) is a dopamine agonist used to treat refractory motor fluctuations in people with Parkinson's disease. Domperidone (brand names: Motilium, Dismotil) is usually started at least two days before apomorphine to control the expected side effects of nausea and vomiting.

Domperidone and the risk of cardiac side effects

In 2014, a review by EU medicines regulators concluded that domperidone is associated with a small increased risk of QT-interval prolongation, serious ventricular arrhythmias, and sudden cardiac death. A higher risk was observed in people older than 60 years, people taking daily oral doses of more than 30 mg, and in those taking other QT-prolonging medicines or cytochrome P450 3A4 inhibitors at the same time as domperidone. As a result of this review, the licensed indication for domperidone was restricted to relief of nausea and vomiting, the licensed dose was reduced, and several contraindications were introduced (see Drug Safety Update article from May 2014 and below* for further details).

Apomorphine with domperidone and the risk of QT-prolongation

Apomorphine can increase the risk of QT-prolongation at high doses.

A review by EU medicines regulators of the safety of concomitant apomorphine and domperidone concluded that health professionals should take the precautions listed above to reduce the risk of QT-prolongation. The risk of QT-prolongation may be increased in people on concomitant apomorphine and domperidone who have certain risk factors, including:

- pre-existing QT-interval prolongation
- serious underlying cardiac disorders such as heart failure
- severe hepatic dysfunction
- significant electrolyte disturbances
- concomitant drug therapy that may increase domperidone levels (eg, cytochrome P450 3A4 inhibitors)

Domperidone: risks of cardiac side effects*

From: Medicines and Healthcare Products Regulatory Agency (MHRA)
Published: 30 May 2014

Indication restricted to nausea and vomiting, new contraindications, and reduced dose and duration of use.

Domperidone is a dopamine antagonist with antiemetic properties.

A European review assessed the benefits and risks of domperidone following continued reports of cardiac side effects. The review confirmed a small increased risk of serious cardiac side effects. A higher risk was observed particularly in people older than 60 years, people taking daily oral domperidone doses of more than 30 mg, and those taking QT-prolonging medicines or CYP3A4 inhibitors at the same time as domperidone. For indications other than nausea and vomiting, the benefits were not considered to outweigh the cardiac risk. Based on the results of this review, the treatment advice for domperidone has been updated.
The overall safety profile of domperidone, and in particular its cardiac risk and potential interactions with other medications, should be taken into account if there is a clinical need to use it at doses or durations greater than those authorised (eg, to control side effects of Parkinson's disease treatment in some patients).
Domperidone should not be used in children under 12 years of age.

Advice for healthcare professionals
Indication
•Domperidone is now restricted to use in the relief of nausea and vomiting
•It should be used at the lowest effective dose for the shortest possible time
Contraindications
•Domperidone is now contraindicated in people:
o with conditions where cardiac conduction is, or could be, impaired
o with underlying cardiac diseases such as congestive heart failure
o receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors
o with severe hepatic impairment
o Patients with these conditions should have their treatment reviewed at their next routine appointment and be switched to an alternative treatment if required

Posology
Oral formulations

•For adults and adolescents over 12 years of age and weighing 35 kg or more, the recommended maximum dose in 24 hours is 30 milligrams (dose interval: 10 milligrams up to three times a day)

Suppository formulation

•Suppositories should only be used in adults and adolescents weighing 35 kg or more, the recommended maximum daily dose in 24 hours is 60 milligrams (dose interval: 30 milligrams twice a day)

Duration of treatment

•The maximum treatment duration should not usually exceed one week

•Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation

Administration of liquid formulations

•Oral liquid formulations of domperidone should only be given via appropriately designed, graduated measuring devices (eg, oral syringes for children and cups for adults and adolescents) to ensure dose accuracy

Appendix 4

Association of British Neurologists Website extract: http://www.theabn.org/news/abn-clinical-research-training-fellowship-2015.html

Domperidone

You will have recently received notification from the MRHA regarding a **LOW RISK** of serious cardiac side-effect (prolonged QTc) with domperidone (see refs below). The ABN has asked the MHRA to provide guidance on the use of this drug in people with Parkinson's disease, but they have not been able to do so. Please click here for recommendations from the ABN.

Copy of letter published on the ABN website:

Dear Colleague,

You will have recently received notification from the MRHA regarding a LOW RISK of serious cardiac side-effect (prolonged QTc) with domperidone (see refs below). The ABN have asked the MHRA to provide guidance on the use of this drug in people with Parkinson's disease, but they have not been able to do so. Members will be aware that a significant proportion of people with Parkinson's disease are only able to tolerate initiation, dose increase, or in some cases maintenance of dopaminergic therapy with domperidone co-administration. For these patients the availability of domperidone as an anti-emetic can make a dramatic difference to their mobility and quality of life. There is no alternative to domperidone in this situation so the balance of risk and benefit should be carefully considered.

The ABN wishes to make the following recommendations: Domperidone SHOULD NOT be prescribed routinely for patients commencing dopaminergic medication, and particularly for those over the age of 60 years or with serious underlying heart conditions such as congestive cardiac failure, severe hepatic impairment or significant electrolyte disturbance.

For Parkinson's patients who develop nausea:

- **Domperidone is the preferred anti-emetic.**
- **A baseline ECG must be performed before prescribing domperidone and the potential benefits / risks of prescribing domperidone discussed with the patient.**
- **If the QTc is greater than 450 milliseconds in a male or more than 470 milliseconds in a female then domperidone should not be prescribed and a cardiology opinion obtained (ECG machines often overestimate, and less commonly underestimate). If a second QT prolonging drug or a strong CYP3A4 inhibitor is to be added then the ECG should be repeated (e.g., ketoconazole or erythromycin).**
- **Patients should be advised to seek prompt medical attention if symptoms such as syncope or palpitations occur.**
- **The prescription of domperidone should not routinely exceed 10mg tds for oral therapy and should be used for as short a period as possible.**
- **It is recommended that the initiation of Apomorphine therapy be covered by domperidone at a dose of 10mg three times a day commencing 2 days before the first dose.**
- **Tolerance usually develops with oral therapy and can develop with Apomorphine, so that a trial of domperidone dose reduction or withdrawal should be regularly considered.**

- Domperidone may also be beneficial in the management of orthostatic hypotension in Parkinson's patients. The same recommendations will apply.
- The initiation of domperidone should be under the recommendation and guidance of the Parkinson's specialist.
- There is no need immediately to withdraw domperidone in any Parkinson's patients currently on this drug. The continued necessity for prescribing domperidone should be reviewed at their next, and every subsequent, Parkinson's clinic review.

How low is the cardiovascular risk?

- Four epidemiology studies [1] [2] [3] [4] have reported on the relation between domperidone and either sudden cardiac death alone, or on serious ventricular arrhythmia and sudden cardiac death as a combined endpoint. The findings from the two most recent studies [1,2] are summarised below.
- Van Noord and colleagues [1] looked at 1304 cases of sudden cardiac death and 13 480 matched controls, of which ten cases were currently exposed to domperidone. For current use of domperidone, the adjusted odds ratio (OR) for a risk of sudden cardiac death was 1.92 (95% CI: 0.78–4.73). Analysis by dose suggested a higher risk for patients prescribed domperidone at higher doses (>30 mg/day), although there were only 4 exposed cases in each group and the 95% confidence intervals overlapped: OR 11.4 (1.99–64.9) for patients prescribed >30 mg/day, compared with 0.99 (0.23–4.23) for patients receiving 30mg/day.
- The study by Johannes and colleagues [2] was the largest and most robust study in terms of exposed cases and included 1608 cases and 6428 controls (proton pump inhibitor [PPI] users), of which there were 169 cases and 482 controls with current exposure to domperidone. Compared with users of PPIs, the OR for current domperidone exposure was 1.44 (1.12–1.86). Stratified analyses by age and sex suggested a slightly higher risk for patients older than 60 years (OR1.47 [1.14–1.91]) compared with those younger than 60 years (OR 1.23 [0.32–4.76]), although the 95% confidence intervals overlapped.

References

1) Van Noord C, ET al. Drug Saf 2010; 33: 1003–14
2) Johannes C, et al. Pharmacoepidemiol Drug Saf 2010; 19: 881-88
3) Stratus SM, et al. Eur Heart Journal 2005; 19: 2007-12
4) De Bruin ML, et al. Br J Clin Pharmacol 2007; 63: 216-23