Frimley Health and Care

National shared care protocol for apomorphine for Parkinson's disease in adult services	
Adapted and adopted for use in (NHS Frimley)	
Agreed by NHS Frimley Medicines Optimisation Group	December 2024
Ratified by NHS Frimley Medicines Board	January 2025
Review date	January 2030

Shared care protocol:

Apomorphine for Parkinson's disease

The content of this shared care protocol was correct as of the date of approval. As well these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the treatment for at least 4 weeks and until optimised.

- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- Check local formulary status and, if accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.
- Adjust the dose prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Take medication as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their prescriber and be aware they should discuss the use of specialist medication with their pharmacist before purchasing any OTC medicines.
- Not to drive or operate heavy machinery if medication affects their ability to do so safely.

- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant

1. Background

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Apomorphine is recommended by NICE for patients with Parkinson's Disease who need more advanced treatment than their initial oral medications.

It is used for treatment of motor fluctuations ('on-off' phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication. The patient's treatment with levodopa, with or without dopamine agonists, should be optimised before starting apomorphine treatment.

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.

2. Indications

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The licensed indications covered by the document are:

- Treatment in adults of motor fluctuations ('on-off' phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication. The patient's treatment with levodopa, with or without dopamine agonists, should be optimised before starting APO-go treatment.

3. Locally agreed off-label use

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Nil

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC)and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Under 18 years of age
- Pregnancy and breast feeding
- Respiratory depression
- Dementia
- Psychotic diseases
- Hepatic insufficiency
- Patients who have an 'on' response to levodopa which is marred by severe dyskinesia or dystonia
- Hypersensitivity to Apomorphine or any excipients of the medicinal product

Cautions:

- Renal, pulmonary or cardiovascular disease
- Persons prone to nausea and vomiting.
- Pre-existing postural hypotension.
- Prolonged QTc interval/ risk of torsade de pointes arrhythmia
- Neuropsychiatric problems

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

Bolus doses for prefilled pens

The daily dose of APO-go varies widely between patients, typically within the range of 3-30mg, given as 1-10 injections and sometimes as many as 12 separate injections per day. It is

recommended that individual bolus injections should not exceed 10mg and the total daily dose should not exceed 100mg.
APO-go pen 30mg/3ml

APO-go POD 100mg/20ml
Infusion doses
Dose range from 1-4mg/hr. Infusions should run for waking hours only. Unless the patient is experiencing severe night-time problems. If overnight treatment is necessary, there should be an overnight period of treatment break of at least 4 hour if clinically possible to prevent the development of tolerance.
It is recommended that the total daily dose of Apomorphine, given either as bolus or an infusion should not exceed 100mg
Subcutaneous injection at the tummy area under the navel, outer aspects of the thighs or upper arms. Injection site should be rotated.
The loading period must be prescribed by the initiating specialist.

6. Pharmaceutical aspects

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Route of administration:	subcutaneous
Formulation:	POD is a 20ml pre-filled cartridge, that patients will find easier to prime (no transfer of liquid etc), as it's a simple chronosleeve that fits over the cartridge, and a quick twist into place on the pump. As it is 20ml (versus 10ml in the PFS), 1 POD will replace 2 PFS, and will have a shelf life of 48hrs from priming.
Administration details:	Apomorphine will be administered through CANE CRONO PA4 20 pump
Other important information:	

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

- **Parkinson's medications** – monitor for unusual undesirable effects or signs of potentiation of effect.

- **Neuroleptics** – There is an 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 (symptoms suggestive of neuroleptic malignant syndrome have been reported rarely with abrupt withdrawal of dopaminergic therapy).

- **Antihypertensive and Cardiac Active Medicinal Products** – Apomorphine may potentiate the antihypertensive effects of these medicinal products.

- **Medicines that could prolong QT interval** – Avoid the administration of Apomorphine with other drugs known to prolong the QT interval.

- **Ondansetron** – avoid concomitant use due to possible increase in hypotensive effect when given with Apomorphine.

- **Domperidone** – may potentiate the antihypertensive effects of these medicinal products. BNF stated that possible increased risk of ventricular arrhythmias when Apomorphine given with domperidone, however this is used prior to initiation of Apomorphine infusion.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations:

- FBC, LFT, U&Es, ESR, BP and Coombs' test
- ECG to establish QTc interval within 12 months for patient who has underlying cardiac history and within 24 months for patients with no cardiac risk factors.

- Domperidone 10mg TDS prescribed for at least 2 days prior to the initiation of Apomorphine.
- Baseline motor function examination (UPDRS Part 3).
- Time taken to walk 6m and to return to starting point (dependent on the patient's ability).

Initial monitoring (including frequency):

- BP (lying and standing) and pulse
- Ongoing ECG monitoring required if apomorphine dose increased or if domperidone dose increased or used in combination with apomorphine.
- Motor function examination (UPDRS Part3) every 20 minutes after sequential doses of apomorphine.
- Time taken to walk 6m and to return to starting point (dependent on the patient's ability).
- Undertake training of the patient/carer in use of the product.

Ongoing monitoring (including frequency):

The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment, and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually.

After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

- After 4 weeks after treatment – monitor ECG to check for QTc prolongation. If clinically indicated, ECG should be undertaken within 12 months of Apomorphine initiation.
- 6-8 weeks after treatment – domperidone therapy may be continued for up to a maximum of 4 days at of a daily dose of up to a maximum of 10mg three times per day.
- Coomb's test every 6 months.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results. Funding for monitoring in primary care has been agreed from 1st July 2024 onwards.

Monitoring and advice	Frequency
• LFTs, FBC, U&Es • Blood pressure	Every 6 months

	The exact frequency of monitoring to be communicated by the specialist in all cases.
If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.	

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

Result	Action for primary care
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance	
Nausea and vomiting	Common particularly when Apomorphine treatment is first initiated, usually as a result of the omission of domperidone Treatment with domperidone 10mg tds 72 hours before the challenge is essential. This will be provided by the specialist.
Transient sedation	Occurs at each dose of Apomorphine at the start of therapy and will resolve after the first few weeks of treatment
Somnolence	Refer to specialist team. A dose reduction or termination of therapy may be considered.
Dyskinesias during 'on' time	Can be severe and may result in discontinuation of treatment. Refer to specialist team.
Sudden sleep onset	Refer to specialist team. A dose reduction or termination of therapy may be considered.
Injection site reaction – subcutaneous nodule formation at injection site, induration, erythema and tenderness.	Severe nodule formation may lead to worsening of symptoms due to erratic absorption of Apomorphine. Rotate injection site daily. Practice good insertion technique • Straight butterfly needles should be inserted at a 45 degree angle to the horizontal plane when sited in the abdomen and at a 45 degree

	angle to the vertical plane when sited in the thigh. • Neria infusion lines are inserted at a 90 degree angle which look like small thumb tacks. • Gentle massage of the injection site on a daily basis by hand or with a hand-held massage device may help in reducing nodule formation.
Localised discomfort at infusion site e.g. irritation, itching, bruising and pain	Rotate injection site daily.
Abnormal LFTs, FBC, U&Es or low blood pressure.	Seek advice from specialist team.

11. Advice to patients and carers

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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:

- Treatment with dopamine-receptor agonists are associated with impulse control disorders, including pathological gambling, binge eating, and hypersexuality. Patients and their carers should be informed about the risk of impulse control disorders. Ergot- and non-ergot-derived dopamine-receptor agonists do not differ in their propensity to cause impulse control disorders, so switching between dopamine-receptor agonists will not control these side-effects.

Patient information resources:

Add links

12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients 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.

APO-go 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 with apomorphine should be made taking into account the benefit of breast-feeding to the child and the benefit of apomorphine to the woman.

13. Specialist contact information

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Mrs Tracey Coltart,
Britannia Specialist Nurse
Mobile number: 07584 675 845
Email: tracey.coltart-britannia@nhs.net
tracey.coltart@britnurse.com

APO-GO 24 hours helpline
Telephone number: 08081964242
Email: customerservices@britannia-pharm.com

Neuro MDT HUB
Telephone Number: 0300 614 7227
Email: fhft.neurocarenav@nhs.net

Neurology Department
Email: fhft.neuromedsecs@nhs.net
Telephone number: 0300 613 2512

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement should be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

15. References

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- Apomorphine hydrochloride | Drugs | BNF | NICE
- Apomorphine SPCs: Search Results - (emc) (medicines.org.uk)

16. Other relevant national guidance

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- Overview | Parkinson's disease in adults | Guidance | NICE Accessed October 2024.

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

Contact details for specialist given in section 13.

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *Frimley* shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

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

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*
Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____Date: _____

Primary Care Prescriber address/practice stamp

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re:

Patient	*[insert Patient's name]*
NHS Number	*[insert NHS Number]*
Identifier	*[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *Frimley,* in conjunction with local acute trusts have classified *[insert medicine name]*as a Shared Care drug, and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which apply
1.	**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** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, 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** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	

3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed. For this reason I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England ‘Responsibility for prescribing between Primary & Secondary/Tertiary care’ guidance (2018) states that “when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and

the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

Primary Care Prescriber signature: _____
Date: _____

Primary Care Prescriber address/practice stamp