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Barnsley, Bassetlaw, Doncaster and Sheffield

Shared Care Protocol

For the Treatment of

Parkinson's disease

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Shared Care Protocol for the treatment of Parkinson's disease

Statement of Purpose

This shared care protocol (SCP) has been written to enable the continuation of care by primary care clinicians of patients initiated on treatment for Parkinson's disease (PD) by secondary care where this is appropriate and in the patients' best interests. Primary care will only be requested to take over prescribing of PD medication within its licensed indication unless specifically detailed otherwise below.

This guideline covers the pharmacological management only, which is only one aspect of the care pathway.

Referral Guidelines

The NICE CKS for patients with suspected Parkinson's disease clearly states:

"Refer all people with suspected Parkinson's disease ***urgently***, and ***untreated*****,** to a specialist with appropriate expertise in movement disorders (such as a neurologist or elderly care physician), for confirmation of the diagnosis and exclusion of alternative diagnoses".

Prompt referral, preferably untreated, is therefore recommended for confirmation of diagnosis, planning management, counselling and education and initiation of therapy.

Procedure for Initiating Shared Care Arrangements

Patients seen in the Neurology or Geriatric Medicine clinic are provided with a personalised care plan outlined in the letter to the GP and copied to the nurse specialist. Nurse specialists would normally assist in titration of medication within limits recommended by the specialist clinician. The specialist clinician will prescribe the first month's medication for patients seen in the outpatient clinic where possible. The nurse specialist will support patients in titrating their doses and primary care clinicians will then be asked to continue prescribing. Changes in treatment (i.e. prescribing of an alternative medication) advised by the nurse specialists or specialist clinician outside the outpatient clinic will be notified in writing to the GP and letters countersigned by the Consultant Neurologist or Geriatrician. Where appropriate, patients will also be offered the opportunity to contact the services directly via email.

Sharing of care assumes communication between the specialist team, GP and patient and/or patient's carers. The shared care arrangements should be explained to the patient/carer and accepted by them.

Specialist education and training and on-going advice and support is available from the Specialist Team.

Responsibilities of specialist clinician

- To provide patient / carer with contact details for support and help if required; both in and out of hours

- To initiate PD treatment in appropriate patients.
- To prescribe the first month's supply (where possible – see Appendix A).
- As per NICE guideline NG71, when starting treatment for people with Parkinson's disease, give people and their family members and carers (as appropriate) oral and written information about the following risks, and record that the discussion has taken place;
    - Impulse control disorders with all dopaminergic therapy (and the increased risk with dopamine agonists). Also see recommendations 1.4.1–1.4.9.
    - Excessive sleepiness and sudden onset of sleep with dopamine agonists. Also see recommendations 1.5.1–1.5.3.
    - Psychotic symptoms (hallucinations and delusions) with all Parkinson's disease treatments (and the higher risk with dopamine agonists). Also see recommendations 1.5.12–1.5.21.

- Nurse specialist will contact the patient by telephone or offer a clinic appointment/home visit for follow up to assist in dose titration. The nurse specialist will support patients in taking their medication as prescribed. The GP will be notified of the outcome of follow up discussions/appointments.
- All patients are provided with contact details of the nurse specialist so they can contact the service if needed before the nurse contacts them.
- To contact patient's primary care prescriber to request prescribing and monitoring under shared care.
- To advise the primary care prescriber regarding continuation of treatment, including the duration of treatment.
- To discuss any concerns with the primary care prescriber regarding the patient's therapy.

Patients with Parkinson's disease should continue to remain under the care of the specialist Neurology/Care of the Elderly Movement Disorders service unless there are exceptional circumstances

Responsibilities of the primary care clinician

- Contact the requesting specialists if concerns in joining in shared care arrangements,
- To report any serious adverse reaction to the appropriate bodies e.g.: MHRA and the referring specialist
- To continue to prescribe for the patient as advised by the specialist
- Ensure monitoring as indicated in the individual monographs within the monitoring section (see Appendix B)
- To inform the specialist if the patient discontinues treatment for any reason
- To seek the advice of the specialist if any concerns with the patient's therapy
- To conduct an annual medication review or more frequent if required.
- In the event that the primary care prescriber is not able to prescribe, or where shared care is agreed but the specialist is still prescribing certain items e.g. hospital only product; the primary care prescriber will provide the specialist with full details of existing therapy promptly by a secure method on request.

Responsibilities of Patients or Carers

- To be fully involved in, and in agreement with, the decision to move to shared care
- To attend hospital and primary care clinic appointments and to bring monitoring information e.g. up-to-date information on current therapy, booklet (if required). Failure to attend will potentially result in the medication being stopped.
- Present rapidly to the primary care prescriber or specialist should the clinical condition significantly worsen.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking medication for PD.
- To read the product information given to them
- To take medication for PD as prescribed.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.

Indication

Drug treatment - indications and recommended treatment regimes

Indications, cautions, contraindications, side effects, doses and formulations are listed in the British National Formulary; however, these guidelines may differ slightly but represent acceptable practice in the UK.

There are occasions when non-adherence to the licensed indications of PD drugs or use of unlicensed preparations may be justified, for instance where the licence indications do not reflect current knowledge or evidence, the indications do not include well proven uses of the drug or the licence indications are over restrictive. The specialist may recommend the use of drugs beyond the licensed indications and will detail this in the correspondence to the primary care clinician who is being asked to take over the prescribing. Wherever the specialist considers it to be indicated and, if appropriate, they will explain the drug's unlicensed status to the patient or carer.

Disease Monitoring

See Appendix B (for drug management of motor symptoms) and Appendix C (for drug management of non- motor symptoms) for advice on monitoring and management of symptoms often present in patients with PD. If patients develop new symptoms that require urgent treatment, e.g. hallucinations, the primary care clinician should seek telephone advice to consider an immediate change in treatment. Abrupt withdrawal of any dopaminergic medication carries a risk of inducing the neuroleptic malignant syndrome. Some symptoms (A) will be common in general practice and may not necessarily be due to PD. Other symptoms (B) are more likely to require specialist input.

Useful aspects of the disease to assess in primary care include:

- Anxiety (A)
- Depression (A)
- Hallucinosis (B)
- Paranoia - obsessive ideation and compulsive behaviour including gambling (B)
- Blood pressure and postural hypotension (A/B)
- General well-being (A)

- Constipation (A)
- Dysphagia (A/B)
- Mobility, including fine finger movements and balance/falls (but also problems with mobility at night) (B)
- Pain (A/B)
- Sexual dysfunction (including hypersexuality in men on dopaminergic treatment) (A/B)
- Skin lesions. Parkinson's disease is associated with a higher risk of skin cancer (not exclusively melanoma). Any suspicious skin lesion should be evaluated by a specialist. (A)
- Sleep problems (A/B)
- PD dementia (B)
- Drooling (B)

NB Specific attention should be paid to the MHRA advice in relation to fibrotic reactions in patients receiving treatment with the ergot derived dopamine receptor agonists (bromocriptine and cabergoline). Chest x-ray, echocardiogram, FBC and biochemistry will be taken at baseline and annually (normally undertaken in secondary care). Contact Parkinson's Disease nurses/Community Neurology Nurses in case of unexplained malaise, persistent cough, breathlessness, chest or abdominal pain or tenderness, heart failure, etc.

In addition, primary care clinicians may occasionally need to undertake blood tests, but if so this will be recommended in writing in a letter from the clinic on a case by case basis. In all cases it is the responsibility of the prescriber to ensure that appropriate monitoring is being carried out. If patients develop new symptoms that require urgent treatment (e.g. hallucinations), the primary care clinician should seek telephone advice (see contacts list).

Dopaminergic medication (regardless whether L-Dopa or dopamine agonist) must not be abruptly withdrawn since this carries the risk of neuroleptic malignant syndrome. There is also a recognised dopamine agonist withdrawal syndrome (DAWS).

Re-Referral guidelines

Patient will always remain under the care of the clinic and will be seen at regular intervals.

Contacts for Support, education and information

	Contact Details	Telephone number	Email
Consultant Neurologists	Prof Oliver Bandmann (Sheffield Teaching Hospitals)	0114 271 3005 (STH) 01302 644597 (DRI)	Oliver.Bandmann@nhs.net
	Dr Richard Grunewald (Sheffield Teaching Hospitals)	0114 271 2306	Richard.Grunewald@nhs.net
	Dr Aijaz Khan (Sheffield Teaching Hospitals)	0114 27 12619	Aijaz.Khan@nhs.net
	Dr Shaun Mohan (Sheffield Teaching Hospitals)	0114 22 68939	shaun.mohan1@nhs.net
	Dr Aaizza Naqvi (Sheffield Teaching Hospitals)	0114 271 3810	aaizza.naqvi@nhs.net
	Dr Rachel Newby (Sheffield Teaching Hospitals)	0114 226 8615 (STH) 01302 644597 (DRI)	rachel.newby1@nhs.net
Consultant in Elderly Medicine	Dr Bahaa Madi (Barnsley Hospital NHS trust)	01226 730000 Ext. 2264	bahaamadi@nhs.net
Sheffield Care of the Elderly Team	Nicolas Samaniego (Consultant) Gemma Burgin (Parkinson's Nurse Specialist)	0114 2714970	nicolas.samaniego@nhs.net g.burgin@nhs.net

Parkinson's disease specialist nurses	The specialist nurse team can be reached via the generic mailbox or via the phone number listed	0114 2711704	sth.parkinsonsnurse@nhs.net
	Tracey Watt, Jane McConville, Coral Mannion (Tickhill Road Hospital, Doncaster)	01302 796877	tracey.watt3@nhs.net coral.mannion@nhs.net
Community based Parkinson's Nurse specialist	Carolyn Turton (South West Yorkshire Partnership NHS Foundation Trust)	01226 645 180	carolyn.turton@swyt.nhs.uk
Community Neurology Nurses (Bassetlaw CCG patients)	Carol Paczkowski Adrienne Cox (Retford Primary Care)	01777 274422	Carol.Paczkowski@nottshc.nhs.uk Adrienne.Cox@nottshc.nhs.uk
Lead Pharmacist	Natasha Hoyle (Sheffield Teaching Hospitals)	0114 2713225	Natasha.Hoyle@nhs.net

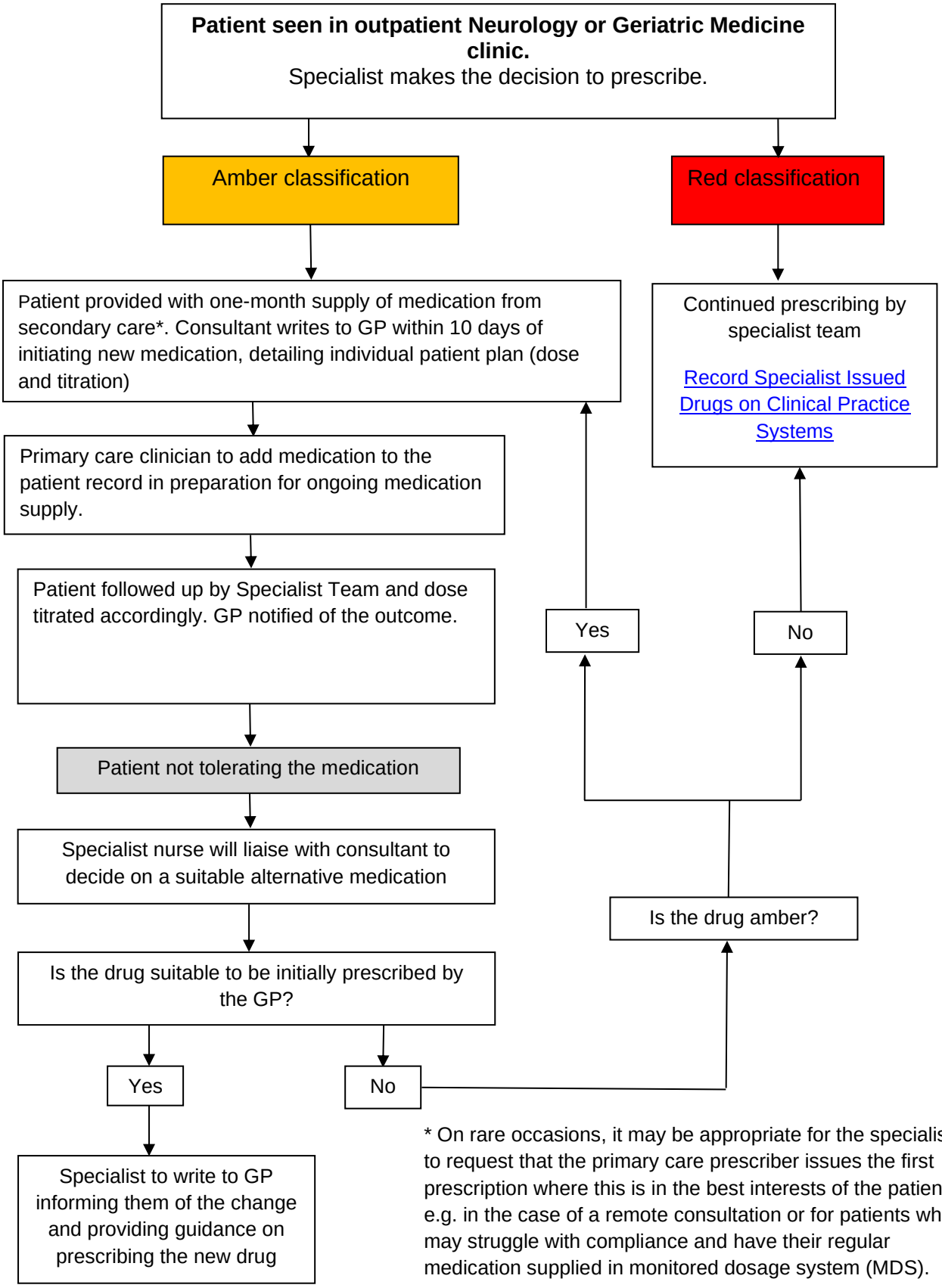
Information is also available online at Parkinson's UK. They also operate a helpline (0808 800 0303) and have local advisors and support groups

Neurology second on call Specialist Registrars are also available to give 24-hour advice.

Neurology website at Sheffield Teaching Hospitals

It will be presumed by the referring specialist that the primary care team is operating under this shared care protocol. Should the primary care prescriber feel unable to act under this shared care protocol they should discuss with the specialist requesting the care in the first instance. If after discussion, they still feel unable to prescribe then the primary care clinician must notify the specialist in writing.

Appendix A – Process for initiating Shared Care



* On rare occasions, it may be appropriate for the specialist to request that the primary care prescriber issues the first prescription where this is in the best interests of the patient e.g. in the case of a remote consultation or for patients who may struggle with compliance and have their regular medication supplied in monitored dosage system (MDS).

Appendix B – Drug management of motor symptoms in Parkinson's disease

All dopaminergic PD drugs are initiated by secondary care. General Practice should not initiate these drugs. On occasion, it may be appropriate for the specialist to request that the primary care prescriber issues the first prescription where this is in the best interests of the patient e.g. in the case of a remote consultation or for patients who have their regular medication supplied in monitored dosage system (MDS).

As per NICE CKS guidance**,** refer all people with suspected Parkinson's disease **urgently**, and ***untreated*****,** to a specialist with appropriate expertise in movement disorders for confirmation of the diagnosis and exclusion of alternative diagnoses".

Drug class	Drug	Traffic light status
Levodopa and associated drugs	Co-beneldopa	Amber
	Co-careldopa	Amber
First line (non-ergotic) dopamine-receptor agonists	Pramipexole	Amber
	Ropinirole	Amber
	Rotigotine	Amber
Second line (ergotic) dopamine-receptor agonists	Bromocriptine	Amber
	Cabergoline	Amber
Third Line dopamine-receptor agonists	Apomorphine	Amber
MAO-B inhibitors	Selegiline	Amber
	Rasagiline	Amber
	Safinamide	Amber
COMT inhibitors	Entacapone	Amber
	Stalevo® (levodopa, carbidopa and entacapone)	Amber
	Opicapone	Amber
Other	Amantadine	Amber

Do not offer anticholinergics to people with Parkinson's disease.

The monographs on the following pages are not comprehensive. The BNF and the SPC remain authoritative.

However, there are occasions when non-adherence to the licensed indications of PD drugs or use of unlicensed preparations may be justified, for instance where the licence indications do not reflect current knowledge, the indications do not include well proven uses of the drug or the licence indications are over restrictive. The specialist may recommend the use of drugs beyond the licensed indications and will detail this in the correspondence to the primary care clinician who is being asked to take over the prescribing. Wherever the specialist considers it to be indicated and, if appropriate, they will explain the drug's unlicensed status to the patient or carer.

Levodopa Drugs

Caution when prescribing levodopa products. There are many different formulations (e.g. dispersible, immediate release, modified release) These formulations will have been carefully selected to optimise symptom control. Extra care should be taken to ensure that the correct product is prescribed.

Dopaminergic medication (regardless whether L-Dopa or dopamine agonist) must not be abruptly withdrawn since this carries the risk of neuroleptic malignant syndrome. There is also a recognised dopamine agonist withdrawal syndrome (DAWS).

Co-beneldopa (benserazide plus levodopa)

SPC available at:
https://www.medicines.org.uk/emc/search?q=levodopa&filters=activeingredients[692]&offset=1&limit=50&orderBy=product&refreshFilters=true
See BNF at: https://bnf.nice.org.uk/drug/co-beneldopa.html

Side Effects: Nausea and vomiting (rarely dose limiting). Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities

Cautions: Severe pulmonary or cardiovascular disease, psychiatric illness, endocrine disorders, history of convulsions or peptic ulcer. Angle closure glaucoma, hepatic impairment, renal impairment. Avoid abrupt withdrawal due to risk of neuroleptic malignant syndrome and rhabdomyolysis.

Drug Interactions: MAOI antidepressants, Antipsychotics may antagonise the effects of Levodopa however atypical antipsychotics are used to treat medication induced psychosis

Switching from one preparation to another: These recommendations can be cited as general guidance, but it is important to access the individual patient for their response.

Immediate release to m/r – 1 capsule substituted for every 100mg of levodopa and given at same dosage frequency. Increase every 2-3 days according to response. Average increase of 50% needed over previous levodopa dose and titration may take up to 4 weeks.

m/r to dispersible – Reduce dose by approx. 30%

Monitoring: None

Co-careldopa (carbidopa plus levodopa)

SPC available at: http://www.medicines.org.uk/emc/medicine/9647
See BNF at https://bnf.nice.org.uk/drug/co-careldopa.html

Side Effects: Nausea and vomiting (rarely dose limiting). Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities

Cautions: Severe pulmonary or cardiovascular disease, psychiatric illness, endocrine disorders, history of convulsions or peptic ulcer. Angle closure glaucoma, hepatic impairment, renal impairment. Avoid abrupt withdrawal due to risk of neuroleptic malignant syndrome and rhabdomyolysis.

Drug Interactions: MAOI antidepressants, Antipsychotics may antagonise the effects of Levodopa however atypical antipsychotics are used to treat medication induced psychosis

Monitoring: None

First line (non-ergotic) dopamine-receptor agonists

Dopaminergic medication must not be abruptly withdrawn since this carries the risk of neuroleptic malignant syndrome. There is also a recognised dopamine agonist withdrawal syndrome (DAWS).

Impulse-control disorder (ICD) can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms such as compulsive gambling, hypersexuality, excessive shopping, binge eating etc. Wherever possible and appropriate, the partner/family of the patients should be made aware of this risk at the time of treatment initiation.

Dopamine-receptor agonists may cause postural hypotension on initiation. Secondary care will advise if ongoing blood pressure monitoring is required for these drugs.

Pramipexole

SPC available at: https://www.medicines.org.uk/emc/search?q=pramipexol
See BNF at:.https://bnf.nice.org.uk/drug/pramipexole.html

Dose and strengths normal release tablets:

Doses and strengths are stated in terms of pramipexole (base); equivalent strengths in terms of pramipexole dihydrochloride monohydrate (salt) are as follows:

Base	88micrograms	180micrograms	350micrograms	700micrograms
Salt	125micrograms	250micrograms	500micrograms	1mg

Dose and strengths prolonged release tablets

Doses and strengths are stated in terms of pramipexole (base); equivalent strengths in terms of pramipexole dihydrochloride monohydrate (salt) are as follows:

Base	260micrograms	520micrograms	1.05mg	1.57mg	2.1mg	2.62mg	3.15mg
Salt	375micrograms	750micrograms	1.5mg	2.25mg	3mg	3.75mg	4.5mg

Patients already taking standard release tablets may be switched to prolonged release tablets overnight, at the same daily dose. After switching, the dose may be adjusted depending on patients therapeutic response

Side Effects: Nausea, constipation, somnolence, dyskinesias, hallucinations and insomnia can occur. Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities. Hypotensive reactions may be disturbing in some patients during the first few days of treatment. Domperidone may be offered to prevent nausea. Note MHRA alert on Domperidone use Hallucinations (mostly visual). Impulsive control disorders and compulsive behaviours

Cautions: Psychotic disorders, severe cardiovascular disease, Renal impairment (prolonged release preparation not suitable for patients with CrCl below 30ml/min – consider standard release tablets instead)

Drug Interactions: Reduction of pramipexole dose should be considered when the following are administered concomitantly: Cimetidine, Diltiazem, Quinidine, Quinine, Ranitidine, Triamterene, Verapamil, Digoxin, Procainamide, Trimethoprim, and Amantadine. Refer to PD specialist nurse or Consultant. Caution should be advised if taking other sedating medication or alcohol. Should not be concurrently administered with drugs which have central dopamine antagonist activity (such chlorpromazine, haloperidol, flupenthixol, metoclopramide etc) however atypical antipsychotics are used to treat medication induced psychosis

Monitoring:
GP and Specialist:. Monitor for Impulse-control disorder (ICD) which can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms (obsessive or compulsive behaviour, confusion, psychosis) If suspected by primary care Contact Parkinson's Disease nurses/Community Neurology Nurses

Ropinirole

SPC available at: https://www.medicines.org.uk/emc/search?q=Ropinirole
See BNF at: https://bnf.nice.org.uk/drug/ropinirole.html

Side Effects: Early therapy patients experienced nausea, somnolence, leg oedema, abdominal pain, vomiting and syncope. Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities. Patients receiving adjunct therapy experienced dyskinesia, nausea, hallucinations and confusion. Decreases in blood pressure have been noted; symptomatic hypotension and bradycardia, occasionally severe, may occur. Domperidone may be offered to prevent nausea. Note MHRA alert on Domperidone use

Cautions: Severe cardiovascular disease, major psychotic disorders, elderly, avoid abrupt withdrawal, dose adjustment may be necessary if smoking started or stopped during treatment.

Drug Interactions: Ropinirole should not be administered with drugs that have dopamine agonist properties, such as phenothiazides, butyrophenones, thioxanthenes or metoclopramide since these may reduce the efficacy of ropinirole, however atypical antipsychotics are used to treat medication induced psychosis. The dose of ropinirole may need to be adjusted when co-prescribed with drugs that affect the cytochrome P450enzyme eg. Ciprofloxacin, theophylline, cimetidine. If HRT is stopped or introduced during treatment with ropinirole, dosage adjustment may be required.

Monitoring: GP and Specialist: Monitor for Impulse-control disorder (ICD) which can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms (obsessive or compulsive behaviour, confusion, psychosis). If suspected by primary care Contact Parkinson's Disease nurses/Community Neurology Nurses

Rotigotine

SPC available at: https://www.medicines.org.uk/emc/search?q=Rotigotine
See BNF at: https://bnf.nice.org.uk/drug/rotigotine.html

Side Effects: Nausea, constipation, dry mouth, diarrhoea, anorexia, dyspepsia, dyskinesias, hallucinations and insomnia can occur. Postural hypotension, peripheral oedema, palpitations, tachycardia, hypotension, hypertension, atrial fibrillation. Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities. Hyperhidrosis, rash (including local reactions to patch), and pruritus.

Cautions: Ophthalmic testing recommended, avoid exposing patch to heat, withdraw gradually,

Drug Interactions: Dopamine antagonists, such as neuroleptics (e.g. phenothiazines, butyrophenones, thioxanthenes) or metoclopramide, may diminish the effectiveness of rotigotine, and co-administration should be avoided. Caution should be advised when patients are taking sedating medicinal products or other CNS (central nervous system) depressants (e.g. benzodiazepines, antipsychotics, antidepressants) or alcohol in combination with rotigotine, due to the possible additive effects.

Monitoring:
GP: Check for skin irritation. Monitor for Impulse-control disorder (ICD) which can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms (obsessive or compulsive behaviour, confusion, psychosis). If suspected by primary care Contact Parkinson's Disease nurses/Community Neurology Nurses

Specialist: 6 monthly LFT, U&E. Patients will be asked about vision abnormalities

Second line (ergotic) dopamine-receptor agonists

Specific attention should be paid to the MHRA advice in relation to fibrotic reactions in patients receiving treatment with the ergot derived dopamine receptor agonists (bromocriptine and cabergoline). Patients should be monitored for dyspnoea, persistent cough, chest pain, cardiac failure and abdominal pain or tenderness

Dopaminergic medication must not be abruptly withdrawn since this carries the risk of neuroleptic malignant syndrome. There is also a recognised dopamine agonist withdrawal syndrome (DAWS).

Impulse-control disorder (ICD) can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms such as compulsive gambling, hypersexuality, excessive shopping, binge eating etc. Wherever possible and appropriate, the partner/family of the patients should be made aware of this risk at the time of treatment initiation.

Dopamine-receptor agonists may cause postural hypotension on initiation. Secondary care will advise if ongoing blood pressure monitoring is required for these drugs.

Bromocriptine

SPC available at: http://www.medicines.org.uk/emc/medicine/28129
See BNF at: https://bnf.nice.org.uk/drug/bromocriptine.html

Side Effects: Nausea may be controlled with domperidone 10mg tds, but in most cases tolerance to nausea develops within 4 weeks. Note MHRA alert on Domperidone use. Hypotensive reactions in some patients may be disturbing in the first few days of treatment. Particular care should be exercised when driving or operating machinery. Tolerance may be reduced by alcohol. Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities. May cause retroperitoneal and pleural fibrosis. See MRHA alert.

Cautions: History of peptic ulcer, Raynaud's syndrome, cardiovascular disease, history of serious mental health disease, acute porphyria.

Drug Interactions: Antipsychotics may antagonise the effects of dopamine agonists however atypical antipsychotics are used to treat medication induced psychosis.

Monitoring:

GP: Unexplained malaise, breathlessness. Monitor for Impulse-control disorder (ICD) which can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms (obsessive or compulsive behaviour, confusion, psychosis). If suspected by primary care Contact Parkinson's Disease nurses/Community Neurology Nurses

Specialist:
- May cause retro peritoneal and pleural fibrosis
- Baseline chest x-ray, ECG, ESR & U&E
- Echo within 3-6 months of starting treatment, then every 6-12 months
- Future monitoring guided by symptomatology

Cabergoline

SPC available at: http://www.medicines.org.uk/emc/medicine/27147
See BNF at: https://bnf.nice.org.uk/drug/cabergoline.html

Side Effects: Hypotensive reactions in some patients may be disturbing in the first few days of treatment. Particular care should be exercised when driving or operating machinery. Tolerance may be reduced by alcohol. Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities. May cause retroperitoneal and pleural fibrosis. See MRHA alert.

Cautions and contraindications: History of peptic ulcer, Raynaud's syndrome, cardiovascular disease, history of serious mental health disease, acute porphyria. Exclude pregnancy before starting and discontinue one month before intended conception.

Drug Interactions: Antipsychotics may antagonise the effects of dopamine agonists however atypical antipsychotics are used to treat medication induced psychosis.

Monitoring:

GP: Unexplained malaise, breathlessness, GP: Unexplained malaise, breathlessness. Monitor for Impulse-control disorder (ICD) which can occur in patients on any dopaminergic medication but is particularly common in patients on dopamine-receptor agonists. The risk appears to correlate with dose and duration of treatment. It is therefore crucial to ask patients on dopamine-receptor agonists at every single visit about ICD-related symptoms (obsessive or compulsive behaviour, confusion, psychosis). If suspected by primary care Contact Parkinson's Disease nurses/Community Neurology Nurses
Specialist:

- May cause retro peritoneal and pleural fibrosis
- Baseline chest x-ray, ECG, ESR & U&E
- Echo within 3-6 months of starting treatment, then every 6-12 months
- Future monitoring guided by symptomatology

Third Line dopamine-receptor agonists

Apomorphine

SPC available at: https://www.medicines.org.uk/emc/search?q=Apomorphine
See BNF at: https://bnf.nice.org.uk/drug/apomorphine-hydrochloride.html#indicationsAndDoses

Side Effects: Apomorphine is a strong emetic. Patients with no contraindications to domperidone should be started on 10mg TDS three days prior to initiation that can be slowly withdrawn over several weeks. Note MHRA alert on Domperidone use. Drowsiness (including sudden onset of sleep) may affect performance of skilled tasks. Patients who are affected should not drive or undertake potentially dangerous activities

Cautions: Pulmonary or cardiovascular disease, history of postural hypotension, susceptibility to QT interval prolongation, neuropsychiatric conditions. Avoid in hepatic impairment and use with caution in renal impairment.

Drug Interactions: Antipsychotics may antagonise the effects of Apomorphine, however atypical antipsychotics are used to treat medication induced psychosis

Monitoring:
GP: Injection site reactions.
Specialist: 6 monthly FBC, LFT, U&Es

MAO-B inhibitors

Selegiline

SPC available at: https://www.medicines.org.uk/emc/search?q=Selegiline
See BNF at: https://bnf.nice.org.uk/drug/selegiline-hydrochloride.html

Side Effects: May cause insomnia if taken in the afternoon or evening. Withdrawal is poorly tolerated in some. Common side effects reported are nausea, constipation, diarrhoea, dry mouth. Less commonly: postural hypotension, dyskinesia, vertigo, sleeping disorders, confusion, hallucinations, arthralgia, myalgia. Rarely: arrhythmias, agitation, headache, micturition difficulties, skin reactions. Chest pain also reported. Side effects of levodopa may be increased. Mouth ulcers with orodispersible tablets.

Cautions: Avoid abrupt withdrawal, gastric and duodenal ulceration, uncontrolled hypertension, arrhythmias, angina, psychosis, hepatic impairment, acute porphyria, renal impairment.

Drug Interactions: Hyperpyrexia and CNS toxicity reported when selegiline given with pethidine. Increased risk of hypertension and CNS excitation when selegiline given with SSRI antidepressants and venlafaxine (e.g. selegiline should not be started until 5 weeks after stopping fluoxetine, avoid fluoxetine for 2 weeks after stopping selegiline – see **selegiline SPC for further information.**). CNS toxicity reported when selegiline given with tricyclic antidepressants. Avoid concomitant use of selegiline with moclobemide.

Monitoring:
GP and Specialist: None

Rasagiline

SPC available at: https://www.medicines.org.uk/emc/search?q=Rasagiline
See BNF at: https://bnf.nice.org.uk/drug/rasagiline.html

Side Effects: Most common side effects reported are; headache, dry mouth, dyspepsia, constipation,angina, postural hypotension, depression, anorexia, abnormal dreams, hallucinations, vertigo, influenza-like symptoms, urinary urgency, leucopenia, arthralgia, conjunctivitis, rash. Rarely; myocardial infarction, and cerebrovascular accident.

Cautions: Avoid abrupt withdrawal, hepatic impairment.

Drug Interactions: Serious adverse reactions have been reported with the concomitant use of selective SSRI's, but also with tricyclic, tetracylic antidepressants and MAO inhibitors as well as with another selective MAO-B inhibitors. Therefore, in view of the MAO inhibitory activity of rasagiline, antidepressants should be administered with caution. Fluoxetine and fluvoxamine should be avoided. At least five weeks should elapse between discontinuation of fluoxetine and initiation of treatment with rasagiline. At least 14 days should elapse between discontinuation of rasagiline and initiation of treatment with fluoxetine or fluvoxamine. Concomitant use with dextromethorphan or sympathomimetics such as those present in nasal and oral decongestants or cold medications containing ephedrine or pseudoephedrine is not recommended

Monitoring:
GP and Specialist: None

Safinamide

Indicated for patients who were either unable to tolerate selegiline/rasagiline or did not benefit from selegiline/rasagiline.

SPC available at: https://www.medicines.org.uk/emc/search?q=Safinamide
See BNF at: https://bnf.nice.org.uk/drug/safinamide.html

Side Effects: Cataract; dizziness; drowsiness; headache; hypotension; injury; nausea; sleep disorders

Cautions: Hypertension (may raise blood pressure); may exacerbate pre-existing dyskinesia (requiring levodopa dose reduction)

Drug Interactions:

Must not be administered along with other MAO inhibitors (including moclobemide). Contraindicated with concomitant use of pethidine. The concomitant use of safinamide and fluoxetine or fluvoxamine should be avoided. Serious adverse reactions have been reported with the concomitant use of selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic/tetracyclic antidepressants and MAO inhibitors . In view of the selective and reversible MAO-B inhibitory activity of safinamide, antidepressants may be administered but used at the lowest doses necessary.

Monitoring:
GP and Specialist: None

COMT inhibitors

Entacapone

SPC available at: https://www.medicines.org.uk/emc/search?q=Entacapone+
See BNF at: https://bnf.nice.org.uk/drug/entacapone.html

Side Effects: Nausea, vomiting, abdominal pain, constipation, diarrhoea, urine may be coloured reddish-brown, dry mouth, dyskinesias; dizziness; rarely hepatitis.

Cautions: Ischaemic heart disease; avoid abrupt withdrawal, hepatic impairment,

Drug Interactions: Entacapone enhances the effect of warfarin. Caution advised by the manufacturer with maprotiline, moclobemide, paroxetine, tricyclic antidepressants and venlafaxine. Avoid concomitant use of Entacapone with non-selective MAOIs.

Monitoring:
GP: None
Specialist: None

Opicapone

SPC available at: https://www.medicines.org.uk/emc/product/7386
See BNF at: https://bnf.nice.org.uk/drug/opicapone.html

Side Effects: Constipation; dizziness; drowsiness; dry mouth; hallucinations; headache; hypotension; movement disorders; muscle complaints; sleep disorders; vomiting

Cautions: Concurrent levodopa dose may need to be reduced; elderly over 85 years (limited information available).

Drug Interactions:

Concomitant use of opicapone with MAO inhibitors (e.g. phenelzine, tranylcypromine and moclobemide) other than those for the treatment of Parkinson's disease is contraindicated. Concomitant use of opicapone and MAO inhibitors for the treatment of Parkinson's disease, e.g. rasagiline (up to 1 mg/day) and selegiline (up to 10 mg/day in oral formulation or 1.25 mg/day in buccal absorption formulation), is permissible. Concomitant use with tricyclic antidepressants and noradrenaline re-uptake inhibitors should be considered with caution.

Monitoring:
GP and Specialist: None

Other

Amantadine

SPC available at: https://www.medicines.org.uk/emc/search?q=Amantadine
See BNF at: https://bnf.nice.org.uk/drug/amantadine-hydrochloride.html

Side Effects: GI disturbance, anorexia, nausea, nervousness, inability to concentrate, insomnia, dizziness, convulsions, hallucinations, feelings of detachment, blurred vision, livedo reticularis, peripheral oedema. Rarely leucopenia and rashes. Hepatic impairment.

Cautions: Congestive heart disease (may exacerbate oedema), confused or hallucinatory states, elderly; avoid abrupt withdrawal in Parkinson's disease;

Drug Interactions: Memantine – increased risk of CNS toxicity.

Monitoring:
GP: None
Specialist: None

Monitoring:
GP and Specialist: None

Appendix C - Drug management of non-motor symptoms in Parkinson's disease

When medicines optimisation /dose adjustments do not improve symptoms or are not clinically appropriate (see NICE NG71, recommendations 1.5)

See NICE guideline on depression in adults with a chronic physical health problem.

Traffic light status of drugs may differ by area – check local classification here: Barnsley, Doncaster and Bassetlaw, Rotherham and Sheffield.

Non motor aspects of disease	Preparation	Dose	Monitoring	Comments
Psychotic symptoms	Quetiapine	12.5mg at night up to maximum 150mg daily	No monitoring required	Caution: may worsen control of motor symptoms of PD.
Refractory psychotic symptoms	Clozapine (Red traffic light)	12.5mg at night to maximum 50mg twice daily	Regular FBC will be monitored by referring team and drug will be issued only on receipt of satisfactory blood test result	Useful in refractory psychotic symptoms associated with PD. Commonly causes drowsiness, hypersalivation and weight gain. Risk of agranulocytosis and myocarditis. See MHRA alert **If constipation occurs during treatment with clozapine (Clozaril, Denzapine, Zaponex), it is vital that it is recognised and actively treated.**
Postural hypotension – consider pharmacological causes	Midodrine	Up to 10mg three times daily	No monitoring required	For postural hypotension. Unlicensed in the UK. Last dose no later than 4 hours before retiring to bed to avoid nocturnal supine hypertension
	Fludrocortisone	Up to 300 microgram per day	Monitor serum potassium for hypokalaemia.	Recommended with in NICE guidance. Unlicensed for this indication in the UK.
	Ephedrine hydrochloride (Off licence use)	15-60mg three times daily	No monitoring required	For postural hypotension. Off licence use.
Daytime hypersomnolence	Modafinil (Off licence use - Red traffic light)	Up to 400mg daily	No monitoring required	Recommended within NICE guidance – exclude reversible causes Unlicensed in the UK for this indication.
Erectile dysfunction	Sildenafil	Initially 50mg approx 1 hour before sexual activity; subsequent doses 25-100mg as single dose.	No monitoring required	For erectile dysfunction.

		Maximum: one dose in 24 hours		
PD dementia complex.	Donepezil	5mg daily at bedtime increasing to maximum 10mg daily	No monitoring required	For PD dementia complex
PD dementia complex/ hallucinosis associated with PD and Dementia with Lewy Bodies	Rivastigmine	Up to 6mg twice daily or a 9.5mg patch.	No monitoring required	For PD dementia complex (licensed indication), hallucinosis associated with PD and Dementia with Lewy Bodies (off licence).
Constipation	Macrogol Sachets	1-3 sachets per day, typically PRN	No monitoring required	For constipation (which is typically part of PD rather than a SE of PD medication)
Rapid eye movement sleep behaviour disorder	Clonazepam	250-500 microgram at night initially		Recommended within NICE guidance. Unlicensed for this indication in the UK.
	Melatonin (modified-release)	2mg at night, can be increased up to 12mg at night	No monitoring required	Recommended within NICE guidance. Unlicensed for this indication in the UK.
Hypersalivation	Glycopyrronium	1-2mg three times daily		Recommended within NICE guidance. Off license for this indication in the UK.
	Botulinum toxin	Administered by hospital		Administered within hospital clinic. Xeomin licensed to treat hypersalivation Other brands of botulinum toxin – Unlicensed for this indication within the UK.