Specialist Pharmacy Service NICE Bites July/August 2017: No 99

A summary of prescribing recommendations from NICE guidance

Parkinson's disease in adults

NICE NG71; 2017

This guideline covers the diagnosis and management of Parkinson's disease in people aged ≥18 years.

Definition of terms				
ADL	activities of daily living			
NMS	neuroleptic malignant syndrome			
COMT inhibitor	catechol-O-methyltransferase inhibitor			
MAO-B inhibitor	monoamine-oxidase B inhibitor			
RBD	rapid eye movement sleep behaviour			
	disorder			
U	unlicensed			

Assessment and diagnosis

- Suspect Parkinson's disease in people presenting with tremor, stiffness, slowness, balance problems and/or gait disorders.
- If Parkinson's disease is suspected, refer people quickly and untreated to a specialist with expertise in the differential diagnosis of this condition.
- Diagnose Parkinson's disease clinically, based on the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria.
- Review the diagnosis at regular intervals of 6 to12 months and reconsider it if atypical clinical features develop.
- See <u>NICE pathway</u> for information on appropriate diagnostic tests.

Information and support

- Communication should aim towards empowering the person with Parkinson's disease to participate in judgements and choices about their own care.
- In discussions, aim to achieve a balance between providing honest, realistic information about the condition and promoting a feeling of optimism.
- Provide both oral and written communication throughout the course of the disease, which should be individually tailored and reinforced as necessary with consistent communication from professionals involved.
- Give family members/carers (as appropriate) information about the condition, their entitlement to a Carer's Assessment and support services available.
- People with Parkinson's disease should have a comprehensive care plan agreed between the person, their family members/ carers (as appropriate), and specialist and secondary healthcare providers.
- Offer people an accessible point of contact with specialist services. This could be provided by a Parkinson's disease nurse specialist.
- Advise people who drive that they should inform the DVLA and their car insurer of their condition when Parkinson's disease is diagnosed.

Treatment and management Motor symptoms

- Before starting treatment discuss the:
 - > person's individual clinical circumstances e.g. symptoms, comorbidities and risks from polypharmacy,
 - person's individual lifestyle circumstances, preferences, needs and goals,
 - potential benefits and harms of the different drug classes. See Table 1.

Table 1: Potential benefits and harms of first-line medicines for motor symptoms

	Levodopa	Dopamine agonists e.g. pramiprexole ropinirole	MAO-B inhibitors e.g. rasagiline selegiline
Motor symptoms	More improvement	Less improvement	Less improvement
ADL	More improvement	Less improvement	Less improvement
Motor complications	More	Fewer	Fewer
Adverse events*	Fewer	More	Fewer

*excessive sleepiness, hallucinations and impulse control disorders

- Antiparkinsonian medicines should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption
- e.g. gastroenteritis, abdominal surgery, to avoid the potential for acute akinesia or NMS.
- Do NOT withdraw antiparkinsonian drugs (so called 'drug holidays') to reduce motor complications because of the risk of NMS.
- In view of the risks of sudden changes in antiparkinsonian medicines, people with Parkinson's disease who are admitted to hospital or care homes should have their medicines:
 - given at the appropriate times, which in some cases may mean allowing self-medication,
 - > adjusted by, or adjusted only after discussion with, a specialist in the management of Parkinson's disease.

First-line treatment

- For people in the early stages of Parkinson's disease:
 - > offer levodopa to people whose motor symptoms impact on their quality of life.
 - consider a choice of dopamine agonists, levodopa or MAO-B inhibitors for people whose motor symptoms do not impact on their quality of life.
- **Do NOT** offer ergot-derived dopamine agonists as first-line treatment. See **Box 1** (page 2).
- When starting treatment give people and their family members/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),
 - excessive sleepiness and sudden onset of sleep with dopamine agonists,
 - > psychotic symptoms (hallucinations and delusions) with all Parkinson's disease treatments (and the higher risk with dopamine agonists).

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Box 1

MHRA guidance – ergot-derived dopamine agonists

- Ergot-derived dopamine agonists should not be given to people who have had fibrosis in the heart, lungs or abdomen. Cabergoline, pergolide and bromocriptine are contraindicated for people with evidence of valve problems, and cabergoline and pergolide are restricted to second-line use in Parkinson's disease.
- Absence of cardiac fibrosis should be verified before treatment is started, and people must be monitored for signs of fibrosis on echocardiography before treatment is started, and then regularly during treatment.
- The risk of cardiac fibrosis is higher with cabergoline and pergolide than with the other ergot-derived dopamine agonists.
 Drug Safety Update: Volume 1, Issue 12; 2008

Adjuvant treatment

- If a person develops dyskinesia and/or motor fluctuations, including medicines 'wearing off', seek advice from a healthcare professional with specialist expertise in Parkinson's disease before modifying therapy.
- Offer a choice of dopamine agonists, MAO-B inhibitors or COMT inhibitors as an adjunct to levodopa for people who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy, after discussing the:
 - person's individual clinical circumstances e.g. their Parkinson's disease symptoms, comorbidities and risks from polypharmacy,
 - person's individual lifestyle circumstances, preferences, needs and goals,
- potential benefits and harms of the different drug classes. See Table 2.
- Choose a non-ergot-derived dopamine agonist in most cases, because of the monitoring that is needed with ergot-derived dopamine agonists. See Box 1.
- Only consider an ergot-derived dopamine agonist as an adjunct to levodopa for people with Parkinson's disease:
 - > who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy, AND
 - > whose symptoms are not adequately controlled with a nonergot-derived dopamine agonist.
- If dyskinesia is not adequately managed by modifying existing therapy, consider amantadine.
- Do NOT offer anticholinergics to people with Parkinson's disease who have developed dyskinesia and/or motor fluctuations.
- Recognise that impulse control disorders can develop in a person with Parkinson's disease who is on any dopaminergic therapy at any stage in the disease course.

- Recognise that the following are associated with an increased risk of developing impulse control disorders:
 - > dopamine agonist therapy,
 - > a history of previous impulsive behaviour,
 > a history of alcohol consumption and/or smoking.
- When starting dopamine agonist therapy, give people and their family members/carers (as appropriate) oral and written information about the following, and record that the discussion has taken place:
 - > the increased risk of developing impulse control disorders, and that these may be concealed by the person affected,
 - > the different types of impulse control disorders, e.g. compulsive gambling, hypersexuality, binge eating and obsessive shopping,
 - > who to contact if impulse control disorders develop,
 - > the possibility that if problematic impulse control disorders develop, dopamine agonist therapy will be reviewed and may be reduced or stopped.
- Discuss potential impulse control disorders at review appointments, particularly when modifying therapy, and record that the discussion has taken place.
- Be aware that impulse control disorders can also develop while taking dopaminergic therapies other than dopamine agonists.

Management and monitoring

- If a person has developed a problematic impulse control disorder, seek advice from a healthcare professional with specialist expertise in Parkinson's disease before modifying dopaminergic therapy.
- Discuss the following with the person and their family members/carers (as appropriate):
 - > how the impulse control disorder is affecting their life,
 - possible treatments, such as reducing or stopping dopaminergic therapy,
 - > the benefits and disadvantages of reducing or stopping dopaminergic therapy. Modify dopaminergic therapy by first gradually reducing any dopamine agonist. Monitor whether the impulse control disorder improves and whether the person has any symptoms of dopamine agonist withdrawal.
- Offer specialist cognitive behavioural therapy targeted at impulse control disorders if modifying dopaminergic therapy is not effective.

Recommendations – wording used such as 'offer' and 'consider' denote the <u>strength of the recommendation.</u>

Drug recommendations – the guideline assumes that prescribers will use a drug's <u>Summary of Product Characteristics</u> (SPC) to inform treatment decisions.

	Dopamine agonists e.g. pramiprexole ropinirole	MAO-B inhibitors e.g. rasagiline selegiline	COMT inhibitors e.g.entacapone tolcapone	Amantadine	
Motor symptoms	In	No evidence			
ADL		No evidence			
Off time**	More off-time reduction	Off-time reduction	Off-time reduction	No studies	
Adverse events	Intermediate risk	Fewer	More	No studies	
Hallucinations	More risk	Lower risk	Lower risk	No studies	
**periods of the day when levododpa is not working well, causing worsening of parkinsonian symptoms					

Table 2: Potential benefits and harms of medicines used as adjuvants to levodopa for motor symptoms

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Managing non-motor symptoms Nocturnal akinesia

- · Consider levodopa or oral dopamine agonists to treat nocturnal akinesia in people with Parkinson's disease. If the selected option is not effective or not tolerated, offer the other instead.
- Consider rotigotine transdermal patches if levodopa and/or oral dopamine agonists are not effective.

Daytime sleepiness

- Advise people with Parkinson's disease who have daytime sleepiness and/or sudden onset of sleep not to drive (and to inform DVLA of their symptoms) and to think about any occupation hazards. Adjust their medicines to reduce its occurrence, having first sought advice from a healthcare professional with specialist expertise in Parkinson's disease.
- Consider modafinil only if a detailed sleep history has excluded reversible pharmacological and physical causes.
- At least every 12 months, a healthcare professional with specialist expertise in Parkinson's disease should review people with Parkinson's disease who are taking modafinil. See NICE Evidence summary: Modafinil for excessive daytime sleepiness in Parkinson's disease.
- Take care to identify and manage restless leg syndrome and RBD in people with Parkinson's disease and sleep disturbance. Parkinson's disease dementia
- Consider clonazepamU or melatoninU to treat restless leg syndrome and RBD if a medicines review has addressed possible pharmacological causes.

Orthostatic hypotension

- If a person with Parkinson's disease has developed orthostatic hypotension, review the person's existing medicines to address possible pharmacological causes, including:
 - > antihypertensives (including diuretics),
 - > dopaminergics,
 - > anticholinergics,
 - > antidepressants.
- Consider midodrine for people with Parkinson's disease and orthostatic hypotension, taking into account the contraindications and monitoring requirements (including monitoring for supine hypertension). See NICE Evidence summary: Midodrine for orthostatic hypotension due to autonomic dysfunction.
- If midodrine is contraindicated, not tolerated or not effective, consider fludrocortisoneU (taking into account its safety profile, in particular cardiac risk and potential interactions with other medicines).

Depression

- For guidance on identifying, treating and managing depression in people with Parkinson's disease, see NICE pathway: Depression
- Also see <u>NICE pathway: Multimorbidity and Social care for</u> older people with multiple long-term conditions.

Psychotic symptoms

- At review appointments and following medicines changes, ask people with Parkinson's disease and their family members/carers (as appropriate) if the person is experiencing hallucinations (particularly visual) or delusions.
- · Perform a general medical evaluation for people with hallucinations or delusions, and offer treatment for any conditions that might have triggered them.
- Do NOT treat hallucinations and delusions if they are well tolerated by the person with Parkinson's disease and their family members/carers (as appropriate).

- Reduce the dosage of any Parkinson's disease medicines that might have triggered hallucinations or delusions, taking into account severity of symptoms and possible withdrawal effects. Seek advice from a healthcare professional with specialist expertise in Parkinson's disease before modifying therapy.
- Consider quetiapine U to treat hallucinations and delusions in people with Parkinson's disease who have no cognitive impairment.
- If standard treatment is not effective, offer clozapine to treat hallucinations and delusions in people with Parkinson's disease. Be aware that registration with a patient monitoring service is needed.
- Be aware that lower doses of quetiapine U and clozapine are needed for people with Parkinson's disease than other indications.
- Do NOT offer olanzapine to treat hallucinations and delusions in people with Parkinson's disease.
- Recognise that other antipsychotic medicines (such as phenothiazines and butyrophenones) can worsen the features of Parkinson's disease.
- See NICE pathway: Dementia.

- Offer a cholinesterase inhibitor*** for people with mild or moderate Parkinson's disease dementia.
- Consider a cholinesterase inhibitor U for people with severe Parkinson's disease dementia.
- Consider memantine U only if cholinesterase inhibitors are not tolerated or are contraindicated.
- For guidance on assessing and managing dementia, and supporting people living with dementia, see NICE pathway: **Dementia**

Drooling of saliva

- Only consider pharmacological management if nonpharmacological management e.g. speech and language therapy, is not available or has not been effective.
- Consider glycopyrronium bromideU to manage drooling of saliva in people with Parkinson's disease. See NICE Evidence summary: Hypersalivation: oral glycopyrronium bromide.
- If treatment with glycopyrronium bromide is not effective, not tolerated or contraindicated e.g. in people with cognitive impairment, hallucinations or delusions, or a history of adverse effects following anticholinergic treatment, consider referral to a specialist service for botulinum toxin AU.
- · Only consider anticholinergic medicines other than glycopyrronium bromide if their risk of cognitive adverse effects is thought to be minimal. Use topical preparations if possible e.g. atropine, to reduce the risk of adverse events.

***Rivastigmine capsules are the only treatment with a UK marketing authorisation for this indication (July 2017). Donepezil, galantamine, and rivastigmine patches are unlicensed for this indication. Informed consent should be obtained and documented.

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Ongoing monitoring and supportive therapies

- People should have regular access to:
 - clinical monitoring and medicines adjustment,
 - a continuing point of contact for support, including home visits when appropriate,
 - > a reliable source of information about clinical and social matters of concern to people with Parkinson's disease and their family members/carers (as appropriate), which may be provided by a Parkinson's disease nurse specialist.

Physiotherapy and physical therapy

- Consider referring people in the early stages of Parkinson's disease to a physiotherapist with experience of Parkinson's disease for assessment, education and advice, including information about physical activity.
- Offer Parkinson's disease-specific physiotherapy for people who are experiencing balance or motor function problems.
- Consider the Alexander Technique for people with Parkinson's disease who are experiencing balance or motor function problems.

Occupational therapy

- Consider referring people in the early stages of Parkinson's disease to an occupational therapist with experience of Parkinson's disease for assessment, education and advice on motor and non-motor symptoms.
- Offer Parkinson's disease-specific occupational therapy for people who are having difficulties with ADL.

Speech and language therapy

- Consider referring people in the early stages of Parkinson's disease to a speech and language therapist with experience of Parkinson's disease for assessment, education and advice.
- Offer speech and language therapy for people with Parkinson's disease who are experiencing problems with communication, swallowing or saliva. This should include:
 - strategies to improve the safety and efficiency of swallowing to minimise the risk of aspiration, such as expiratory muscle strength training,
- strategies to improve speech and communication, such as attention to effort therapies.
- Consider referring people for alternative and augmentative communication equipment that meets their communication needs as Parkinson's disease progresses and their needs change.

Nutrition

- Consider referring people with Parkinson's disease to a dietitian for specialist advice.
- Discuss a diet in which most of the protein is eaten in the final main meal of the day (a protein redistribution diet) for people with Parkinson's disease on levodopa who experience motor fluctuations.
- Advise people with Parkinson's disease to avoid a reduction in their total daily protein consumption.
- Advise people with Parkinson's disease to take a vitamin D supplement. See <u>NICE pathway: Vitamin D increasing</u> <u>supplement use in at-risk groups</u>, <u>NICE pathway: Preventing falls in older people</u>, and <u>NICE pathway: Osteoporosis</u>.
- Do NOT offer creatine supplements to people with Parkinson's disease.
- Advise people with Parkinson's disease not to take over-thecounter dietary supplements without first consulting their pharmacist or other healthcare professional.

Neuroprotective therapies

- Do NOT use: vitamin E co-enzyme Q10^a dopamine agonists^a MAO-B inhibitors^a
- ^a except in the context of clinical trials

Advanced Parkinson's disease

- Offer people with advanced Parkinson's disease best medical therapy, which may include intermittent apomorphine injection and/or continuous subcutaneous apomorphine infusion.
- Do NOT offer deep brain stimulation to people with Parkinson's disease whose symptoms are adequately controlled by best medical therapy.
- Consider deep brain stimulation for people with advanced Parkinson's disease whose symptoms are not adequately controlled by best medical therapy. See <u>NICE interventional</u> <u>procedures guidance: Deep brain stimulation for Parkinson's</u> <u>disease.</u>

Palliative Care

- Offer people with Parkinson's disease and their family members and carers (as appropriate) opportunities to discuss the prognosis of their condition. These discussions should promote people's priorities, shared decision-making and patient-centred care.
- Offer people and their family members/carers (as appropriate) oral and written information about the following, and record that the discussion has taken place:
 - > progression of Parkinson's disease,
 - > possible future adverse effects of medicines used in advanced Parkinson's disease,
 - > advance care planning, including Advance Decisions to Refuse Treatment (ADRT) and Do Not Attempt Resuscitation (DNACPR) orders, and Lasting Power of Attorney for finance and/or health and social care,
 - options for future management,
 - > what could happen at the end of life,
 - > available support services, e.g. personal care, equipment and practical support, financial support and advice, care at home and respite care,
 - > when discussing palliative care, recognise that family members/carers may have different information needs from the person with Parkinson's disease.

Resources

BMJ Infographic: Managing symptoms of Parkinson's disease: http://www.bmj.com/content/bmj/suppl/2017/07/27/bmj.j1951.DC1/ro gg130417.w1.pdf

Patient information leaflets: https://www.parkinsons.org.uk/

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