



PARKINSON'S DISEASE (PD)

Top tips for MURs

- Check that the patient understands why medication has been prescribed and address any compliance issues
- Counsel patient on the need to take medication regularly to maintain adequate control and never to stop abruptly (risk of neuroleptic malignant syndrome or acute akinesia¹)
- Check whether the patient is registered with a specialist movement disorder clinic for regular reviews of their PD; this also ensures access to physiotherapy, speech / language support & occupational therapy
- Refer patients on levodopa with "on-off" effects - periods of normal movement or dyskinesias alternating with loss of mobility or "freezing"
- Counsel patients on signs / symptoms that need referral (see red flags overleaf)
- Counsel patients on common side effects and how they should be managed (see overleaf)
- Counsel patients taking levodopa to have regular eye examinations (↑ risk of glaucoma¹)
- Advise patients to report any new or changing moles without delay, there is an increased risk of malignant melanoma in PD
- Warn patients on treatment with dopamine receptor agonists or levodopa about the risk of impulse control disorders (ICD), including pathological gambling, binge eating and hypersexuality (make a note of this warning in the patient's medication record)
- Advise patients who drive that they should have informed the DVLA and their car insurer of their condition at the time of diagnosis
- Assess whether the patient is taking any medications which could exacerbate tremor or PD e.g. certain antipsychotics, antiemetics, diltiazem and antidepressants, refer if concerned
- Signpost patient to self-help leaflets and websites (e.g. 'Parkinson's UK')
- Report any relevant adverse drug reactions to the Yellow Card Scheme

Pathophysiology of Parkinson's Disease

Parkinson's disease is a progressive neurodegenerative condition resulting from the death of the dopamine-containing cells and increased levels of acetylcholine in the substantia nigra². People with Parkinson's Disease commonly present with slowness (bradykinesia), rigidity and rest tremor³. Although Parkinson's Disease is predominantly a movement disorder, other non-motor impairments frequently develop such as depression, dementia, psychosis and sleep disturbance².

Autonomic disturbances and pain may later ensue, as the condition progresses to cause significant disability and handicap with impaired quality of life for the affected person. Family and carers may also be affected indirectly.

Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 or more days, with several alcohol free days)
- Advise patients who smoke of the benefits of stopping smoking and how to access enhanced smoking cessation services in community pharmacy and GP practices. Note for smokers who are receiving rasagiline/ropinirole, dose changes may be required if smoking is stopped (CYP1A2 metabolism)¹
- Counsel patient on healthy eating, exercise & weight loss (if BMI > 25kg/m²) – reduce saturated fat and salt intake, avoid salt substitutes, increase oily fish intake, complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake and recommend 5 portions of fruit and vegetables a day
- Advise good sleep hygiene in patients with sleep disturbance

How do medications to treat parkinson's disease work?

Levodopa (either as Madopar®, Sinemet® or Duodopa® which is levodopa gel administered with a portable pump directly into the duodenum or upper jejunum by permanent tube)	Converted to dopamine in the brain by decarboxylation increasing brain-dopamine concentrations. Levodopa is given in combination with a peripheral dopa-decarboxylase inhibitor (benserazide or carbidopa).
Dopamine receptor agonists (e.g. ropinirole, rotigotine, pramipexole and apomorphine)	Mimic the dopamine molecule so bind directly to post-synaptic dopamine receptors within the corpus striatum.
MAO-B inhibitors (rasagiline, selegiline)	Irreversible inhibition of MAO-B and inhibition of re-uptake of dopamine into the pre-synaptic neurons.
Antimuscarinics (orphenadrine, procyclidine, trihexyphenidyl) Not used first line due to unacceptable side effects	Competitive antagonists of the binding of acetylcholine to muscarinic receptors in substantia nigra resulting in decreased levels. Useful in drug-induced parkinsonism.
Amantadine	Mostly used now to improve dyskinesias in later disease not to treat PD itself. Weak antagonist of NMDA type glutamate receptor which increases dopamine release and blocks dopamine reuptake.
Catechol-O-Methyl Transferase (COMT) inhibitors (entacapone, tolcapone (rarely used))	Prevents the peripheral breakdown of levodopa, by inhibiting COMT, allowing more levodopa to reach the brain.
Stalevo® (combination of Sinemet® and entacapone)	As for separate entries.



Red flags that need referral

- Fibrotic reactions with ergot-derived dopamine-receptor agonists (dyspnoea, persistent cough, chest pain, cardiac failure, abdominal pain or tenderness)
- Severe fluctuations or 'on-off' phenomena
- Compulsive behaviour (e.g. gambling, binge eating and hypersexuality)
- Signs of liver disorder (anorexia, nausea, vomiting, fatigue, abdominal pain, dark urine, pruritus) - tolcapone
- Rapid deterioration in mobility, increased number of falls (especially in early disease)
- Hallucinations / dementia / depression / cognitive decline especially early in disease history
- Suspected malignant melanoma (new or changing moles)

What are the common side effects to look out for?

Common side effects	Recommendation
Nausea, vomiting, constipation, weight changes, taste disturbances, dry mouth, anorexia, hiccups, diarrhoea	Advise patient that this is usually short term, nausea and vomiting may be treated with a short course of domperidone if severe and medication can be taken with food until nausea abates. Refer patients taking entacapone who experience diarrhoea. Refer to prescriber / Parkinson's Disease nurse specialist (PDNS) if not tolerated.
Sudden onset of sleep	Advise patient about serious risk of driving or working with machinery if affected. Refer to prescriber / PDNS for dose reduction/specialist advice. Advise on sleep hygiene measures if appropriate.
Motor complications - dystonia, dyskinesia and chorea	Advise patient that many of these side effects are short term and refer to prescriber / PDNS if not tolerated.
Impulse control disorders (pathological gambling, binge eating and hypersexuality)	Refer to prescriber / PDNS, dose should be reduced or withdrawn.
Arrhythmias, palpitations or postural hypotension. Postural hypotension can occur with dopamine agonists particularly in the first few days of treatment	Advise that postural hypotension may resolve and to reduce caffeine intake gradually. Refer to prescriber / PDNS.
Arthralgia, myalgia, muscle cramps	Advise that these may be side effects or symptoms of PD - refer to prescriber / PDNS if problematic. Recommend simple analgesia if appropriate.
Rhabdomyolysis, red/brown discolouration of urine (entacapone) and symptoms of liver disease (tolcapone)	Refer to prescriber / PDNS.
Drowsiness, fatigue, dementia, insomnia, depression, anxiety	Insomnia due to stimulant effect of amantadine can be reduced by avoiding administration after 4pm. Discuss sleep / exercise routine (see lifestyle issues)
Confusion, cognitive impairment, hallucinations, dizziness, sleep disturbance	Refer to prescriber / PDNS.
Livedo reticularis (rose-coloured lower extremities) e.g. with amantadine	Refer to prescriber / PDNS.
Peripheral oedema	Refer to prescriber / PDNS-dose may need to be reduced.

Potential drug interactions?

Drugs used to treat parkinson's disease interact with many other medications including antidepressants (SSRIs & MAOIs), memantine, opioid analgesics, oestrogens, progestogens, sympathomimetics, warfarin as well as other parkinson's drugs – **See BNF Appendix 1: Interactions for more details**

Where can you find more information?

- Drug used in parkinsonism and related disorders – BNF sub-section 4.9
- *Evidence-based management of neurological disease and neurological disorder; advancing your practice* distance learning packs that can be found on WCPPE website (<http://www.wcppe.org.uk>)
- NICE guidance CG35 Parkinson's disease can be found on NICE website (<http://www.nice.org.uk>)
- Clinical Knowledge Summaries- (<http://www.cks.nice.org.uk>)
- National Prescribing Centre (<http://www.nps.nhs.uk>)
- SIGN guideline 113: Diagnosis and pharmacological management of Parkinson's disease (<http://www.sign.ac.uk>)

References

1. Summary of product characteristics (SPC) for: Madopar 50mg/12.5mg tablets, Adartrel 0.25,0.5 and 2mg tablets and Azilect 1mg tablets: www.medicines.org.uk/emc/medicine
2. Neurological disorders: advancing your practice (level 2), CPPE 2010
3. Evidence based management of neurological disease, NICPLD, 2012