PARKINSON'S MEDICATION AND MANAGEMENT

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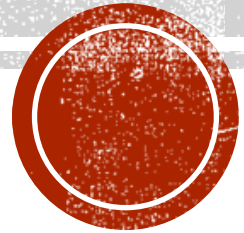

LEVODOPA

- Contained in Sinemet (generics Fairmed) immediate and prolonged release with Carbidopa
- Contained in Stalevo (generics of Stalevo include Sandoz, Sastravi- made by Actavis) with Carbidopa and Entacapone
- Levodopa also contained in Madopar dispersible with Benserazide
- Levodopa is broken down into dopamine in the brain
- Carbidopa/Benserazide prevents the breakdown of Levodopa before it reaches the brain by inhibiting decarboxylase

- Sinemet CR is used for those with night-time symptoms or to prevent 'wearing' off
- Madopar is believed to have a faster onset of action- likely benefits for those suffering from early morning or afternoon akinesia, or who exhibit delayed on or wearing off phenomena
- Various doses of Sinemet and the dose will be decided by your neurologist based on your needs/symptoms

- Levodopa needs to cross the blood-brain barrier in order to work
- Avoid taking medication with heavy meals, particularly ensuring to avoid protein rich meals
- If diet is high in protein may also reduce how well medication works
- If possible take 30-60 minutes before meal

- Levodopa acts as a protein-building block and is absorbed in a similar way to other proteins
- If taken with too much protein, it may not be absorbed before the protein in the food and may 'stick to the food' and undergo digestive breakdown reducing how well it may work

LEVODOPA CONTINUED

- Dyskinesias may occur with levodopa- particularly after taking for many years and is associated with the end of the 'honeymoon' period or disease progression
- Dyskinesias usually occur during peak clinical effect i.e. 1-2 hours after taking levodopa
- End of dose wearing off may be associated with disease progression, protein interactions, need for dose change or timing

- **Timing-** Levodopa must be taken at strict times, as agreed with your neurologist, stick to same time each day
- **Missed dose-** do not take an extra dose to make up for a forgotten dose
- **Side effects-** GI Upset, Loss of appetite, Light-headedness, Lowered blood pressure, Confusion, Dyskinesia (particularly later treatment)

- Coating protects medications from early breakdown in the stomach sometimes and where possible tablets should be taken whole unless difficulty swallowing
- Sinemet CR must be taken whole as with all modified release tablets
- If a tablet has a score line in the middle- this usually means that the coating is designed that the tablet can be halved at this point
- Unless strictly necessary and discussed with your doctor or pharmacist, tablets should not be halved

ENTACAPONE

- Entacapone is available as an individual tablet under the brand Comtan and is contained in Stalevo as part of a combination with Levodopa/Carbidopa
- Used as an add-on for levodopa/carbidopa with end-of-dose fluctuations
- Works by inhibiting COMT (catechol-O-methyl transferase)
- COMT breaks down dopamine- hence entacapone is intended to increase the availability of dopamine
- In early weeks of taking levodopa dose may need to be changed as entacapone increases effect of Levodopa, and of Levodopa side effects (may decrease amount of levodopa per dose or increase timing between doses)

- **Side effects-** GI upset, urine discolouration, dyskinesias, compulsive behaviours and has been linked to heart events such as angina but not heart attacks
- **Timing –** to be taken with Levodopa/Carbidopa- timing is determined by the timing of these
- **Missed Doses-** Do not take a double dose of entacapone (Comtan)- do not take the missed dose- resume taking when next dose of levodopa is due
- **Food-** can be taken with or without food- food does not affect absorption

- Some risk of liver problems- caution needed in those with liver disease

RASAGILINE

- Available as the branded Azilect or generics including Krka, Teva, Rowa, Clonmel, Ratiopharm
- Rasagiline may be used alone (or with a COMT inhibitor) in early Parkinson's disease to delay the need for levodopa.
- Rasagiline may also be used as an add-on to Levodopa treatment if end of dose fluctuations occur
- Works by inhibition Monoamine Oxidase B which is believed to help reduce breakdown of dopamine in the brain
- **Side effects-** headache, dyskinesias (when used as an add-on), hallucinations, abnormal dreams, flatulence, orthostatic hypotension (drop in blood pressure when standing- occurs more frequently in first two months)
- **Timing –** Taken once daily with or without levodopa- take at a similar time each day
- **Missed Doses-** Do not take a double dose, take the next dose normally when it is due to taken
- **Food-** can be taken with or without food- food does not affect absorption



SELEGILINE

- Currently only available as the branded Eldepryl
- Selegiline may be used alone (or with a COMT inhibitor) in early Parkinson's disease to delay the need for levodopa.
- Selegiline may also be added if on-off symptoms or dyskinesias occur with maximum levodopa therapy
- Selegiline was once used to treat depression
- Works by inhibition Monoamine Oxidase B which is believed to help reduce breakdown of dopamine in the brain
- Addition of selegiline may make it possible to reduce levodopa by up to 30%
- **Side effects-** sleeping disorders, dry mouth, dyskinesias, slow heart rate, nausea
- **Timing –** Can be taken as a single dose in morning or split dose in morning and lunchtime
  - If taken in evening or night can keep you awake
- **Missed Doses-** Take as soon as you remember within 24 hours, do not take a double dose
- **Food-** can be taken with or without food- food does not affect absorption

PRAMIPEXOLE

- Available as Mirapexin, Miramel, Oprymea, Sifrol, Pramipexole Teva, Pramipexole Accord in a variety of doses and as immediate release and controlled release.
- Pramipexole works as a dopamine agonist mainly activating the D3 receptors
- Approved for use as monotherapy or as an add-on to levodopa when end of dose or on-off fluctuations occur
- Used to treat motor symptoms
- Also used to treat restless legs syndrome

- **Side effects-** nausea, dyskinesia, hypotension (particularly at the beginning and if dose increased too fast), dizziness, drowsiness, insomnia, constipation, hallucination, headache and compulsive behaviours
- **Timing –** Take at a similar time each day (usually once daily controlled release or three time daily immediate release)- do not break or crush- swallow whole
- **Missed Doses-** For controlled release- take within 12 hours of time dose was due, if more than 12 hours leave this dose out- do not take a double dose and take next tablet when due
  - For immediate release- leave dose out completely and continue on normal dose schedule- do not take a double dose to make up
- **Food-** can be taken with or without food

ROPINIROLE

- Available as immediate release (Requip) or controlled release tablets (Requip Modu-tab or Rolpryna SR)
- Used as an initial monotherapy to delay levodopa treatment or as an add-on to levodopa when end of dose or on-off fluctuations occur
- Works as a dopamine agonist i.e. acts in the brain on receptors that need dopamine to control movement in the place of dopamine
- **Most linked to compulsive behaviours**

- **Side effects-** GI upset, compulsive behaviour, drowsiness, dizziness, hallucinations, dyskinesias (when used with levodopa)
- **Timing –** Take at a similar time each day- modified release once daily or immediate release three times daily
- **Missed Doses-** Do not take extra tablets to make up for missed dose- speak to your doctor if you have missed ropinirole for one day or more for next steps
- **Food-** taking with food will help reduce gastrointestinal side effects- recommended for immediate release- but can be taken with or without food
- Swallow whole with a glass of water- do not break or crush these tablets

RIVASTIGMINE

- Available as patches and capsules. Brand is Exelon, a number of generics are available
- Patches are only approved for use in Alzheimer's disease
- Capsules are used for the treatment of dementia (memory loss) related to Parkinson's disease to improve activities of daily living
- It is known as an cholinesterase inhibitor and reduces acetylcholine levels which are associated with cognitive decline

- **Side effects-** GI upset, weight loss, dizziness, fatigue, nightmares
- **Timing –** Usually taken twice daily, similar time each say, swallow whole with a glass of water
- **Missed Doses-** Wait until next dose, do no take double dose
- **Food-** Take with food



AMANTADINE

- Not currently 'licenced' in Ireland. Imported from the UK
- Brand of capsules Symmetrel – also available in liquid form
- It is now known exactly how it works in the brain but has been found to increase dopamine release from the brain
- Not believed to remain effective in the long-term
- Withdrawal/stopping should be done slowly

- **Side effects-** dry mouth, GI upset, excessive sweating, swollen ankles, possible compulsive behaviours, dizziness, nightmares, hallucinations, headaches, insomnia
- **Timing –** Try to take at the same time each day- usually taken twice daily
- **Missed Doses-** Take as soon as you remember, unless near time of you next dose- do not take a double dose
- **Food-** can be taken with or without food- Amantadine may increase the effects of alcohol



PUMPS

- Duo dopa is administered as a gel via an intestinal pump
- This is often reserved for advance Parkinson's
- Advantages include better control of symptoms and disadvantages include carrying pump around and invasive procedure for insertion

- Apomorphine is available in a pre-filled pen and pre-filled syringe
- Advantages include portability, less 'off periods', improved quality of life, can act as rescue treatment
- Disadvantages include sudden sleepiness, possible nausea, vomiting and dizziness
- Apomorphine is not on the Parkinson's list of core treatments from the HSE so is not paid for by the HSE



PATCHES

- Neupro Patch (rotigotine)
- Dopamine agonist
- Once-a-day
- Makes brain think there is more dopamine than there is by activating receptors for dopamine
- No meal-time effects, patch can get wet, provide drug release for 24 hours
- May cause drowsiness, compulsive behaviours, involuntary movements, weight gain



OVERDOSE

- If you accidentally take too much of your medications, contact your pharmacist immediately for specific advice
- If you realise immediately after taking your medication it may be appropriate to make yourself sick
- If it occurs outside your local pharmacy hours, you may contact a late night pharmacy or a doctor-on-call service for advice

‘HONEYMOON PERIOD’

- The ‘honeymoon period’ refers to the first few years of treatment (usually with Levodopa) where the treatment is the most effective and motor control is often well maintained with treatment
- During the ‘honeymoon period’ it is important to keep up with lifestyle factors including exercise
- As the ‘honeymoon period’ begins to end there is a possibility of experience ‘off effects’ where the effects of the levodopa/carbidopa begins to wear off before the next dose is due and dose changes may be necessary
- Your neurologist will be best placed to discuss this with you and it is important to report any ‘off effects’ or symptoms so that your medication regimen can be optimised at all points



TO START OR NOT TO START

- If you are unsure about when or whether to start medication treatment for your Parkinson's it is important to have an open and honest conversation with your neurologist
- The answer to this question depends on the individual
- As a pharmacist, I cannot recommend delay or initiation of treatment as this will need to be discussed on a case-by-case basis with your doctor
- In discussions with your doctor, it is important to ensure your voice is heard and perhaps have a written list of your thoughts, concerns and questions with you on your doctor visits.
- It is important not to be fearful of treatment and when you begin treatment to take the medication as prescribed and if you begin to experience side effects or feel the need to change treatment to speak to your doctor or pharmacist
- Some information on when to start levodopa is including in the following link:
- https://evidence.nihr.ac.uk/alert/when-is-it-best-to-start-the-parkinsons-drug-levodopa/



BLISTER PACKING

- Blister packing is not advisable ideally especially for levodopa products due to strict timing for taking
- If medication is difficult to manage/remember, speak to your community pharmacist who may be able to advise further- important that if tablets are being sorted into pillboxes that it is done accurately
- Risk of dropping incorrect medication into same time of day
- If pillboxes/blister packs are used ideally a separate container/package for Parkinson's medication should be used to facilitate accurate timing
- Blister pack from pharmacies may be difficult to open/ pop tablets out- particularly if experiencing tremor
- Possible to purchase a pillbox easy to open and bring into pharmacy to have pharmacist prepare medications e.g. wide, clips, buttons
- Some pillboxes can be purchased with an alarm attaches- very useful if forgetting to take medicines at the correct times



Alarm
Clip opening/closing



Push/Button Opening





Smaller openings

Examples of pillboxes currently available online



Slide opening

B VITAMINS

- B Vitamins protect the nervous system in particular B1, B6 and B12
- All are water soluble meaning they are not stored in the body for long periods
- Possible benefit of B vitamins supplementation on PD but limited evidence to date
- B1 (Thiamine)
- B2 (Riboflavin) Believed to protect nervous system in PD and have some role in the disease pathway
- B3 (Niacin) Some protection of nerves at low doses but higher doses can cause further damage
- B5 (Pantothenic Acid) Low levels associated with PD
- B6 (Pyridoxine) dietary intake may reduce risk of developing PD, impacts on how levodopa works, higher B6 levels associated with less neuropathy
- B7 (Biotin) Limited links
- B9 (Folic Acid) Benefits of folic acid supplementation for neuroprotection
- B12 (Cyancobalmin)



VITAMIN B1

- High dose thiamine associated with improved motor and non-motor symptoms but again limited evidence
- Believed to work through restorative and neuroprotective routes.



VITAMIN B12

- Vitamin B12 deficiency is common in people with PD with neuropathy
- Vitamin b12 levels decline over the course of PD
- Low B12 levels have been associated with peripheral neuropathy, cognitive impairment, and more rapid rate of disease progression in PD
- Vitamin B12 is a neuro-protective vitamin
- Vitamin B12 levels can also be reduced by Levodopa
- Emerging studies show some potential benefit to Vitamin B12 to help to slow PD progression but not yet confirmed in human studies



COMPULSIVE BEHAVIOURS

- Dopamine is related to reward seeking behaviour
- Serotonin usually suppresses the reward seeking behaviour
- Such behaviours include compulsive online shopping, gambling, compulsive eating, hoarding, collecting or repairing a specific type of item
- Ropinirole is most associated with this and this is due to the way in which it works although all dopamine replacement therapy carries some risk
- Ropinirole works by activating the dopamine receptors in the brain
- If you are starting on ropinirole there is a risk that you may develop these symptoms
- Inform your family and close friends that you are starting this ropinirole and ask them to check in with you about potential compulsive behaviours or out of character behaviour
- If compulsive behaviours occur contact your doctor immediately, do not stop the medication until after you have spoken with the doctor
- Management may include changing dose, changing medication and psychological support
- Little is known about the risk factors for developing compulsive behaviours although it is believed that men, younger people with Parkinson's, those who have Parkinson's a long time, smokers and those with a family history of gambling or addiction may be more likely to develop compulsive behaviours.



CONSTIPATION

- Constipation- particularly if severe or chronic may reduce medication absorption and can as a result reduce absorption
- If constipation occurs consult with your pharmacist as soon as you notice on management options which will range from diet changes to gentle liquid laxatives to stronger laxatives



PAINKILLERS

- The common non-prescription painkillers are suitable
- Paracetamol is the safest option
- Codeine containing products are appropriate but may increase risk if constipation
- Ibuprofen may be good for musculoskeletal pain- needs to be taken with food
- Prescription painkillers will depend on the type of pain
- Diclofenac (Difene, Diclac) may be used commonly for muscle or joint pain and will need to be taken with food
- For pain associated with cramping or spasm, you will need to discuss options with your doctor
- For prolonged musculoskeletal pain, physiotherapy or exercise may be consider as an option
- More information: https://www.parkinsons.org.uk/sites/default/files/2018-09/FS37%20Pain%20in%20Parkinson%27s_WEB.pdf



GRAPEFRUIT

- Grapefruit and grapefruit juice affects how the body breaks down some medications due to an effect on certain liver enzymes (known as CYP3A4 interactions)
- If you have been advised to avoid grapefruit/grapefruit juice it applies to both the fruit and the juice
- You may need to check if served fruit salads contain grapefruit before eating these
- It should state on the fine print of your medication labels if you need to avoid grapefruit but if you are unsure you can ask your pharmacist
- The same interaction does not occur with normal oranges or orange juice
- However if grapefruit needs to be avoided then so do Seville Oranges (often used to make marmalade)
- There are no such interactions with celery, although you may have been advised to avoid celery
- This is as celery has a high water content but may reduce the need to urinate
- Eating Celery in moderation, however, should be ok



NAUSEA/ANTIEMETICS

- If experiencing vomiting after taking your medication, contact your pharmacist for specific advice on whether or not you need to take more medications. This depends on the time from last dose to vomiting and how quickly each individual medication is absorbed
- Domperidone (Motilium) which can be bought without prescription is not known to cause any adverse Parkinson's effects
- Some of the anti nausea tablets which may be prescribed to you may cause dyskinesias/freezing so should be avoided in Parkinson's
- Always ask your doctor and pharmacist if a nausea medication prescribed is ok for you to take with Parkinson's
- The medications to be avoided include: Prochlorperazine (Stemetil- also used for vertigo), Metoclopramide (Maxolon), Promethazine (Phenergan)

- A safe option that is available on prescription is Cyclizine (Valoid)



HAYFEVER

- Always check with your pharmacist to ensure no drug interactions between allergy medication and any other medications- although interactions with hayfever medications are uncommon
- No key interactions with some of the common hayfever tablets with the medications listed on the first slide
- Common hayfever medications include: Cetirizine (Cetrine, Anti-Hist, Zirtek), Loratadine (Lorat, Claritin), Fexofenadine (Telfast), Chlorpheniramine (Piriton)
- However, allergy medications have a risk of drowsiness in particular Chlorpheniramine (Piriton) and sometimes with the others which may compound tiredness or falls risk associated with Parkinson's if this applies
- In these cases, try the 'non-drowsy' options Cetirizine or Loratadine first
- Some allergy medications are combination products, the most common is Zirtek Plus (Cetirizine and Pseudoephedrine)
- Pseudoephedrine should not be taken if you are taking Rasagiline or Selegiline
- In all cases, if you have any doubt about anything you take without prescription, ask you pharmacist

Document of Interest: Medications to avoid: https://www.apdaparkinson.org/wp-content/uploads/2018/05/APDA-Meds_to_Avoid.pdf

Some of the listed drugs will be American-specific but still useful resource



COUGHS AND COLDS

- Many Cold and Flu medications contain Pseudoephedrine which should not be taken if you are taking Rasagiline or Selegiline
- It is important to inform the pharmacy staff that you are taking medications and asking to speak to the pharmacist when buying cold and flu medication
- Paracetamol is safe in all cases and this includes normal Lemsip, but not all Lemsip as some Lemsip products contain pseudoprime (e.g. Lemsip Cold and Flu capsules, Lemsip sinus and flu)
- Cough bottles such as Exputex and Bronchostop should be ok with Parkinson's medications but it is important to check if you have any other medical conditions
- Ideally avoid cough bottles that can cause drowsiness due to already possible drowsiness side effects

SLEEPING TABLETS

- Sleeping tablets are used for the treatment of insomnia and have benefits in helping an individual fall asleep but not necessarily to stay asleep
- Sleeping tablets can sometimes cause ‘hangover effects’ the following morning due to residual drowsiness
- Risks with taking sleeping tablets if waking in the middle of the night are predominantly associated with residual drowsiness in the morning (as it wont have had the whole night to clear from the body)
- Residual drowsiness is associated with increased falls risk
- Given increased falls risk if experience gait issues or tremor, this residual drowsiness further increases the falls risk and is best avoided where possible
- If falling asleep is an issue, it would be worth discussing with your doctor about the benefits and risks of sleeping tablets although if staying asleep is the problem, then unfortunately, sleeping tablets are likely to have less to offer
- Possibility to alter timing of Parkinson’s medication or to use controlled release Sinemet at night, under advice of your neurologist, to attempt to maintain sleep. This will be case-by-case and should only be done upon consultation with your neurologist
- Useful information on sleep from American Parkinson’s Disease Association: https://www.apdaparkinson.org/what-is-parkinsons/symptoms/sleep-problems/



Exercise and dopamine

- It is perceived by some that exercising uses up the dopamine in a levodopa product
- There is no strong scientific evidence of this
- In fact, some studies have found that moderate exercise can improve the efficacy of levodopa
- Exercise can help your body use the natural dopamine in your brain more efficiently- this is not using it up but making the most of the dopamine
- In some cases exercise may reduce required doses of Parkinson's medications but if exercising for long periods e.g. intense, long hikes or marathons, then increased doses may be needed
- The best person to discuss how your exercise may impact your medication needs with is your consultant
- Exercise is important for Parkinson's and the type and intensity of exercise that will be best depends on your interests, fitness and ability
- Some small studies have found that exercise can delay progression of Parkinson's

REF: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4366306/
https://movementdisorders.onlinelibrary.wiley.com/doi/abs/10.1002/mds.21346
https://www.parkinson.org/Understanding-Parkinsons/Treatment/Exercise/Neuroprotective-Benefits-of-Exercise

ANTIDEPRESSANTS

- Depression may be an symptom of Parkinson's Disease
- Exercise can increase serotonin and dopamine production
- Depression is most often linked to low levels or serotonin in the brain but there is also a role of low dopamine levels
- The SSRI antidepressants (e.g. citalopram, sertraline, paroxetine, fluoxetine) have the most evidence for use in Parkinson's
- Some Medications will interact with antidepressants so it is important to always check with your pharmacist or doctor e.g. escitalopram (Lexapro) interacts with Rasagiline (Azilect)
- MAOIs (e.g. Phenelzine) are ideally avoided due to interactions with some Parkinson's medications
- Some recent studies have expressed that antidepressants may slow progression of Parkinson's Disease in particular the Tricyclic Antidepressants such as Nortriptyline, however, evidence for this remains limited

REF: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5459691/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677475/



QUESTIONS?

- What are the best meds/vitamins/probiotics for constipation & PD?
- Can an Irish pharmacy import a drug available elsewhere with the EU?
- The Jigsaw puzzle of medication needs fine tuning: who is best capable of same? The pharmacist, the neurologist, the GP or the patient?



DIABETES TABLETS- ARE THEY SLOWING THE PROGRESSION?

- An small study published in October 2020, found that the risk of diabetic patients developing Parkinson's Disease may be reduced with certain types of diabetic medication i.e. the DPP4 inhibitors e.g. Sitagliptin (in Januvia and Janumet), Linagliptin (in Trajenta and Jenadueto), Sitagliptin (Onglyza) and/or GLP-1 agonists e.g. Dulaglutide (Trulicity), Liraglutide (Victoza)
- No difference for other diabetic medications including insulin was found
- Currently little evidence on what the impact of diabetic medication is on current Parkinson's Disease
- A study on the use of Exenatide, a GLP-1 agonist, licenced for diabetes found that it reduced the severity of PD
- The repurposing of diabetic medications for use to slow progression of PD, particularly the GLP-1 agonists has become an area of interest for pharmaceutical companies but it remains early days

REF: Brauer, R et al. (2020). Diabetes medications and risk of Parkinson's disease: a cohort study of patients with diabetes, Brain, 43(10); 3067–76, https://doi.org/10.1093/brain/awaa262
Foltynie, T., & Athauda, D. (2020). Repurposing anti-diabetic drugs for the treatment of Parkinson's disease: Rationale and clinical experience. *Progress In Brain Research*, 493-523. doi: 10.1016/bs.pbr.2019.10.008