Clinical Resource Guide:
Parkinson's Disease Medication Management

INTRODUCTION TO PARKINSON'S DISEASE MEDICATION MANGAEMENT

This guide has been thoughtfully created for hospice clinicians, serving as a vital tool to navigate the intricacies associated with managing Parkinson's disease during end-of-life care. As individuals with Parkinson's transition into hospice, the effective management of their symptoms requires a nuanced approach. This resource is designed to equip hospice clinicians with the latest information, evidence-based strategies, and practical insights to optimize pharmacologic interventions, ensuring the highest quality of life for patients in their final stages. Additionally, the guide emphasizes the importance of deprescribing when appropriate, acknowledging the delicate balance between symptom management and minimizing medication burden in the hospice setting.

Pharmacist Corner Objectives

1.) Review medication management of Parkinson's disease, emphasizing the following:
   a. Transitioning to an alternative for Rytary®
   b. Medication administration in patients with difficulty swallowing
2.) Review rationale for deprescribing Parkinson's disease pharmacotherapy

PHARMACOLOGIC MANAGEMENT IN HOSPICE

Medications form the cornerstone of managing PD symptoms. Medications include:

PHARMACOLOGIC TREATMENT STRATEGIES FOR TREATING PARKINSONS

Carbidopa/Levodopa formulations

- The most effective medication, used to replace dopamine, thus alleviating motor symptoms
- Challenges include difficulties in consistent administration, potential issues related to dysphagia or decreased gastrointestinal motility, and possible adverse effects like confusion or hallucinations

Medication	Name	Formulation(s)	Notes
Carbidopa/ Levodopa	Sinemet®	• IR tablet • ER tablet • Oral disintegrating	• Versatile, can be administered in multiple different ways • Most cost-effective carbidopa/levodopa formulation
	Dhivy®	• Scored immediate release tablet	• No considerable benefit over generic carbidopa/levodopa formulations
	Duopa®	• Enteral suspension	• Immediate release carbidopa/levodopa can be crushed and administered in slurry or suspension (see below)
	Rytary®	• Extended-release capsule	• Administration challenges in patients with dysphagia • **Expensive, convert to immediate release tabs**

PHARMACOLOGIC TREATMENT STRATEGIES FOR TREATING PARKINSONS (CONTINUED)

Dopamine Agonists

- Stimulate dopamine receptors in the brain
- Similar challenges as carbidopa/levodopa in inconsistent administration and potential side effects

Medication	Name	Formulation(s)	Notes
Pramipexole	Mirapex®	• IR tablet	• **Indications**: monotherapy or in combo for slowness, stiffness, tremor • **Side effects**: nausea, edema, confusion, compulsive
	Mirapex ER®	• ER tablet	
Ropinirole	Requip®	• Tablet	• **Indications**: Combo therapy for slowness, stiffness, tremor • **Side effects**: nausea, edema, confusion, compulsive
	Requip® XL	• Tablet	
Apomorphine	Apokyn®	• Injection	• Used as adjunct therapy for "off" periods • **Onset**: 10 minutes; **Duration**: 90 minutes
	Kynmobi®	• Sublingual film	• Dosed up to five times/day • Can result in significant nausea, often required anti-nausea medication daily for 3 days before starting

COMT-Inhibitors

- Little to no direct effect on symptoms, works by prolonging the effect of levodopa by inhibiting metabolism
- Common side effects include dyskinesia, confusion, hallucinations, discoloration of urine (reddish brown), diarrhea

Medication	Name	Formulation(s)	Notes
Entacapone	Comtan®	• Immediate release	• **Indications**: for motor fluctuations, not used without levodopa • **Dosing**: Typically 4-8 doses/day
Tolcapone	Tasmar®	• Immediate release	• FDA mandates blood test monitoring due to liver abnormalities; considered last line therapy
Carbidopa/ Levodopa/ Entacapone	Stalevo®	• Tablet	• Combination tablet is more convenient, but does not result in improved efficacy • Maximum of eight tablets/day
Opicapone	Ongentys®	• Capsules	• Dosed 50mg orally at bedtime • Combination therapy w/levodopa for "off" time

Amantadine

Medication	Name	Formulation(s)	Notes
Amantadine	Symmetrel®	• Capsules • Tablets • Syrup	• **Indications**: Monotherapy for slowness/stiffness, combination w/levodopa for levodopa-induced dyskinesia
	Gocovri®	• ER capsules	• **Indications**: combination w/levodopa for levodopa-induced dyskinesia; "off" episodes in PD
	Osmolex®	• ER tablets	

MAO-B Inhibitors

- Can be used early in disease as monotherapy or as an adjunct to other medications
- Common side effects include nausea, dry mouth, lightheadedness, constipation, insomnia

Medication	Name	Formulation(s)	Notes
Selegiline	Eldepryl®	• Tablets	• **Indications**: Monotherapy for slowness/stiffness, and tremor; adjunct for motor fluctuations
	Zelapar®	• Orally disintegrating	• **Indications**: Adjunct for motor fluctuations

Rytary® to Sinemet® Conversion:

While recommendations exist for the conversion from Sinemet® to Rytary®, there are no official manufacturer guidelines from Rytary® to Sinemet®. However, based on a suggested conversion resulting in a 70% increase in levodopa in the Rytary® group, a similar decrease could be implemented when converting to Sinemet®, as illustrated below:

Rytary® Regimen	Total Daily Levodopa Dose Post-Conversion
23.75mg/95mg: 3 caps three times/day	**400mg-549mg/day**
23.75mg/95mg: 3 caps four times/day	**550mg-749mg/day**
36.25mg/145mg: 3 capsules three times/day	**750mg-949mg/day**
48.75mg/195mg: 3 capsules three times/day	**950mg-1249mg/day**
48.75mg/195mg: 4 capsules three times/day	**2340mg/day**
61.25mg/245mg: 3 capsules three times/day	**2205mg/day**

Use in Patients with Dysphagia:

For patients with dysphagia who have lost the ability to safely and/or consistently swallow medications, and for whom therapy with carbidopa/levodopa is continued, but commercially available suspension is cost-prohibitive, consider the following:

1.) Convert carbidopa/levodopa formulation to immediate release tablet
2.) Allow tablet to disperse in water (1-5 minutes) or crush tablet
3.) Administer with an oral syringe or mix with applesauce or a soft puree.
4.) Consider dose adjustment vs. symptom management based on patient response

ADDITIONAL MEDICATION CONSIDERATIONS

Managing off time in Parkinson's disease involves addressing periods when medication effectiveness wanes, and symptoms re-emerge. During these off times, individuals may experience a return of motor symptoms, such as tremors, stiffness, and impaired mobility. To effectively manage off time, healthcare providers often reassess medication schedules, consider adjusting dosages, or explore alternative medications. Additionally, incorporating non-pharmacologic interventions, such as physical therapy or lifestyle modifications, can play a crucial role in minimizing the impact of off time on daily functioning. Tailoring a comprehensive approach that combines medication adjustments with holistic strategies is key to optimizing the management of off time in individuals with Parkinson's disease, promoting better quality of life and functional independence.

Deprescribing Requip (ropinirole) or entacapone in patients with advanced Parkinson's disease experiencing increased off time can be a strategic decision based on several considerations. Firstly, as the disease progresses, patients may develop motor fluctuations and dyskinesias that are less responsive to certain medications. Requip, a dopamine agonist, may contribute to dyskinesias and has been associated with impulse control disorders in some cases. Deprescribing it can help mitigate these side effects.

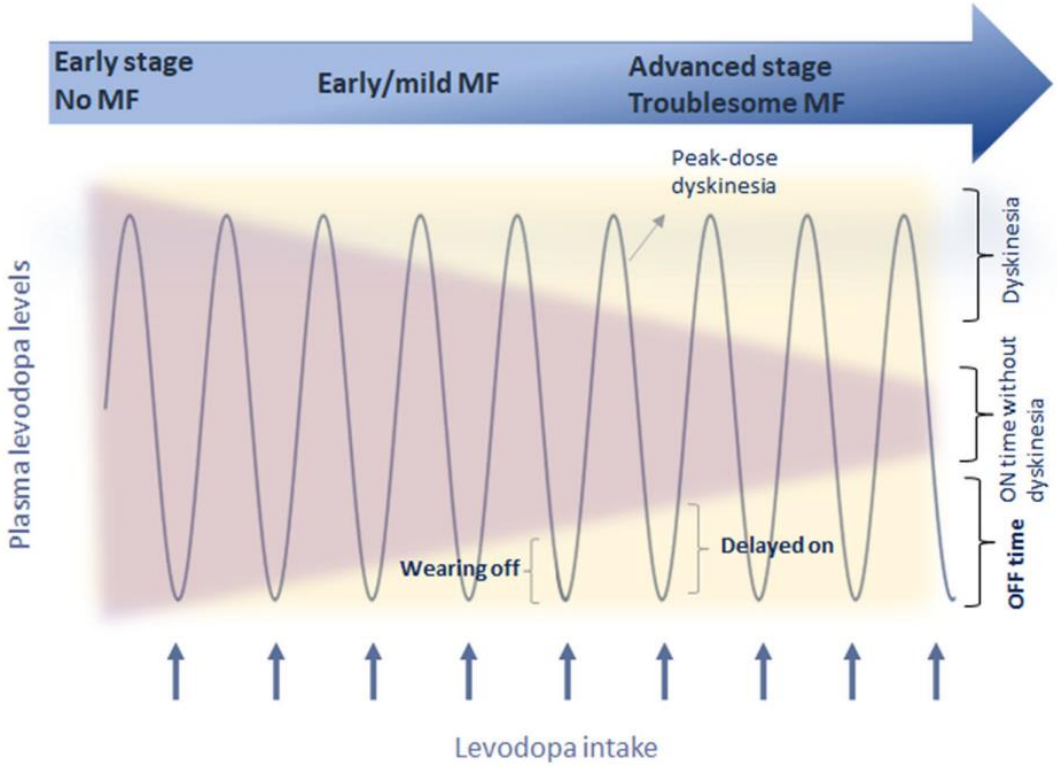

Fig. 1 Motor complications appearance over the disease course. *MF* motor fluctuations

Entacapone, a COMT inhibitor commonly used to prolong the effects of levodopa, may lose effectiveness in advanced stages of the disease due to diminishing levodopa responsiveness. Continued use may not provide significant benefits and could expose patients to unnecessary side effects. Additionally, in some cases, deprescribing medications becomes essential to simplify drug regimens, reduce polypharmacy-related complications, and enhance overall medication adherence. Individual patient response and careful monitoring should guide the deprescribing process, ensuring optimal symptom management and improved quality of life. Always, such decisions should be made in consultation with the patient and the hospice team.

SUMMARY

The Clinical Resource Guide on Parkinson's Disease Medication Management is a valuable tool for hospice clinicians, offering insights into the nuanced management of Parkinson's disease in end-of-life care. This guide provides clinicians with the latest information, evidence-based strategies, and practical insights to optimize pharmacologic interventions. Emphasizing the delicate balance between symptom management and minimizing medication burden, the guide highlights the importance of deprescribing when appropriate. It addresses medication management objectives, including transitioning between medications and reviewing the rationale for deprescribing. The pharmacologic treatment section outlines various medications and considerations for effective management. Overall, the guide advocates for a tailored, holistic approach to enhance the quality of life and functional independence of individuals in the hospice setting.

References:

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