PALLIATIVE PEARLS
BY ENCLARA PHARMACIA

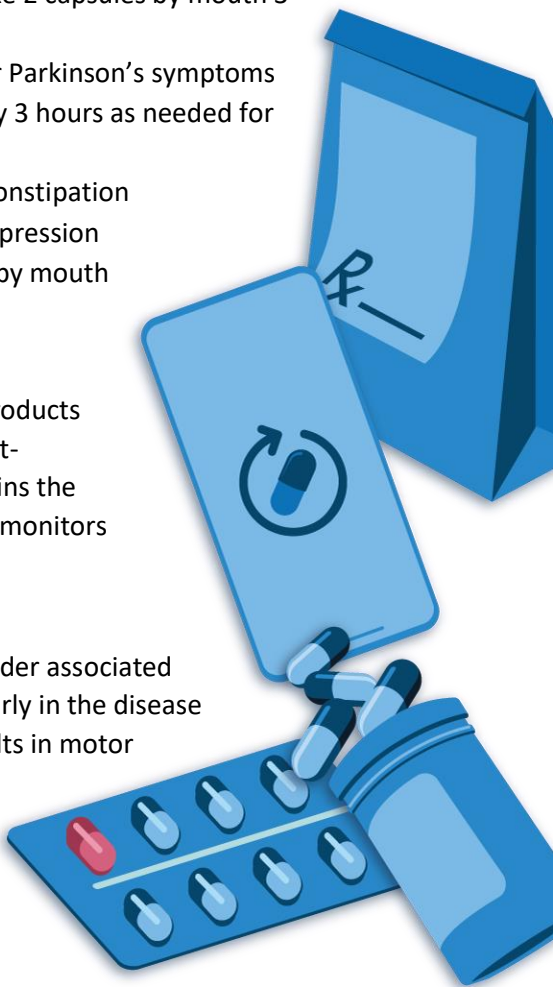
Parkinson's Disease Symptom Management: Converting Between Common Products | May 2021

Patient Case

SN is a 76-year-old female with a primary diagnosis of Parkinson's Disease with depression and hypertension as comorbid conditions. She lives at home with her son who is the primary caregiver. SN was recently admitted to hospice.

Current medications:

- Carbidopa-levodopa extended-release (Rytary®) 48.75-195mg; Take 2 capsules by mouth 3 times daily for Parkinson's symptoms
- Ropinirole (Requip®) 2mg; Take 1 tablet by mouth 3 times daily for Parkinson's symptoms
- Morphine (Roxanol®) 20mg/ml; Take 0.25ml (5mg) by mouth every 3 hours as needed for pain
- Bisacodyl (Dulcolax®) 5mg; Take 1 tablet by mouth every day for constipation
- Sertraline (Zoloft®) 50mg; Take 1 tablet by mouth every day for depression
- Losartan-hydrochlorothiazide (Hyzaar®) 50/12.5mg; Take 1 tablet by mouth every day for high blood pressure



SN's Parkinson's symptoms (tremor, bradykinesia, and rigidity) have been successfully managed on Rytary and Requip for the past 3 months. Both products are not on the hospice's formulary and the team is currently reviewing cost-effective alternatives. SN has no unresolved issues at this time and maintains the ability to swallow without difficulty. Her son is an attentive caregiver that monitors her treatment plan to ensure she adheres to her medication regimen.

PARKINSON'S DISEASE OVERVIEW[1]

Parkinson's disease is a common and slowly progressing neurological disorder associated with death of dopaminergic neurons in the substantia nigra of the brain early in the disease process. Dopamine regulates movement and a decrease in dopamine results in motor symptoms that worsen over time. Motor symptoms include bradykinesia, muscular rigidity, resting tremor, and postural and gait impairment.

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Medications for the symptomatic relief of Parkinson's disease are initiated with the goal of improving function and quality of life. The mainstay of treatment for motor symptoms include medications that enhance intracerebral dopamine concentrations or stimulate dopamine receptors. Levodopa and/or dopamine agonists are the most common of these therapies. There are several products available in these classes; some are costly, presenting an opportunity to explore more cost-effective options when feasible. Discussed in detail below are the most requested dose conversions: From Rytary to Sinemet and from Requip to Mirapex.

RYTARY TO SINEMET CONVERSION[2-4]

Levodopa:[2-4]

Levodopa is the metabolic precursor of dopamine and is thought to relieve symptoms of Parkinson's disease when converted to dopamine in the brain. Levodopa is most commonly found in combination with carbidopa in the below products. Carbidopa inhibits levodopa conversion to dopamine in the periphery allowing for larger amounts of levodopa to cross the blood-brain barrier for conversion to dopamine. Formulations of levodopa and carbidopa are also available with entacapone, which further increase plasma levels of levodopa by inhibiting a major metabolizing enzyme in the periphery, catechol-O-methyltransferase (COMT).

Carbidopa-levodopa products:

- Sinemet® immediate-release tablets
- Stalevo® (includes entacapone) immediate-release tablets
- Parcopa® orally disintegrating tablets
- Duopa® enteral suspension
- Sinemet® CR extended-release tablets
- Rytary® extended-release capsules

Dosages of Rytary® and Sinemet® are not interchangeable. Available manufacturer guidance provides information on conversions FROM Sinemet® TO Rytary® (see bulleted guidance below) but not FROM Rytary® TO Sinemet®. Despite the lack of explicit direction on conversions from Rytary® to Sinemet®, the current manufacturer guidance, along with an appropriate patient assessment, can still aid the healthcare team in determining a potential starting dose of Sinemet®.

Upon review of the bulleted guidance below, note the suggested daily dosages for conversion to Rytary® represent an increase in levodopa at an average of 70%, so it makes sense to employ a similar percent decrease in levodopa in the Rytary® dose when making the switch to the more cost-effective Sinemet®. Alternatively, one could identify where the current Rytary® dose falls closest to in the bulleted guidance and target a Sinemet® dose in the corresponding levodopa range.

Conversion from immediate-release Sinemet® to Rytary®:

- Total Daily Dose (TDD) of levodopa in Sinemet®: 400mg to 549mg
  - Recommend Rytary®: 23.75mg/95mg; 3 capsules taken 3 times daily (TDD of levodopa: 855mg)
- TDD of levodopa in Sinemet®: 550mg to 749mg
  - Recommend Rytary®: 23.75mg/95mg; 4 capsules taken 3 times daily (TDD of levodopa: 1,140mg)
- TDD of levodopa in Sinemet®: 750mg to 949mg
  - Recommend Rytary®: 36.25mg/145mg; 3 capsules taken 3 times daily (TDD of levodopa: 1,305mg)
- TDD of levodopa in Sinemet®: 950mg to 1,249mg
  - Recommend Rytary®: 48.75mg/195mg; 3 capsules taken 3 times daily (TDD of levodopa: 1,755mg)
- TDD of levodopa in Sinemet®: Equal to or greater than 1,250mg
  - Recommend Rytary®: 48.75mg/195mg; 4 capsules taken 3 times daily (TDD of levodopa: 2,340mg) OR 61.25mg/245mg; 3 capsules taken 3 times daily (TDD of levodopa: 2,205mg)

REQUIP TO MIRAPEX CONVERSION:[10, 11]

Dopamine Agonists:[5-9]

Dopamine agonists exert their activity by binding to dopamine receptors in the brain. Their action at dopamine receptors is thought to lessen motor symptoms in Parkinson's disease. Dopamine agonists have successfully been used as monotherapy, as well in combination with regimens consisting of levodopa. Studies evaluating the addition of dopamine agonists have led to 20-30% reductions in levodopa dosages, and improvement in disabling complications.[9]

Dopamine agonists include:

- Ergot-derivatives
  - Parlodel® (bromocriptine) tablets and capsules
- Non-ergot derivatives
  - Mirapex® (pramipexole) regular-release tablets
  - Mirapex® ER (pramipexole) extended-release tablets
  - Requip® (ropinirole) regular-release tablets
  - Requip® XL (ropinirole) extended-release tablets
  - Neupro® (rotigotine) transdermal patch

Manufacturer guidelines for the conversion from Requip® to Mirapex® are not available however several limited studies have proposed a conversion factor of 1:4 from pramipexole to ropinirole. Study results suggest conversion factors could facilitate rapid switches between dopamine agonists in patients with Parkinson's disease, and using a 1:4 conversion ratio resulted in the fewest discontinuations and dosage adjustments. [10, 11]

PATIENT CASE ASSESSMENT & RECOMMENDATIONS

Recall that SN has responded well to her regimen of Rytary® and Requip® and the hospice team would like guidance on potential cost-effective alternatives.

Rytary®:

- SN's total daily dose of levodopa in Rytary® is 1170mg which would represent about a 70% increase from 700mg
    - Solve for "x" where 1.7x = 1170mg
- Alternatively, when reviewing the manufacturer guidance on Sinemet® to Rytary® conversions, 1170mg of levodopa in Rytary® more closely corresponds with the second bullet, restated here:
    - TDD of levodopa in Sinemet®: 550mg to 749mg
        - Recommend Rytary®: 23.75mg/95mg; 4 capsules taken 3 times daily (TDD of levodopa: 1,140mg)
- Carbidopa-levodopa (Sinemet®) is available in 25/250mg tablets with a recommended dosing frequency of 3 or 4 times daily[2]
- Recommend a rapid (i.e., overnight) switch to carbidopa-levodopa (Sinemet®) 25/250mg tablet; Take 1 tablet by mouth 3 times daily

Requip®:

- SN's total daily dose of Requip® is 6mg; Using a 1:4 pramipexole:ropinirole conversion ratio, we estimate a target dose of Mirapex 1.5mg daily
- Pramipexole (Mirapex®) is available in 0.5mg tablets with a recommended dosing frequency of 3 times daily[6]
- Recommend a rapid (i.e., overnight) switch to pramipexole (Mirapex®) 0.5mg tablet; Take 1 tablet by mouth 3 times daily

Additionally, it is recommended that SN be monitored closely following the switch to the new regimen for both efficacy and safety purposes. Monitor for the emergence or worsening of motor symptoms such as bradykinesia, rigidity, tremor and postural impairment to identify patient tolerance and need for dose adjustments.

To read more about Parkinson's disease symptom management, see our Palliative Pearls case Parkinson's Disease Psychosis: Patient Case and Brief Review.

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