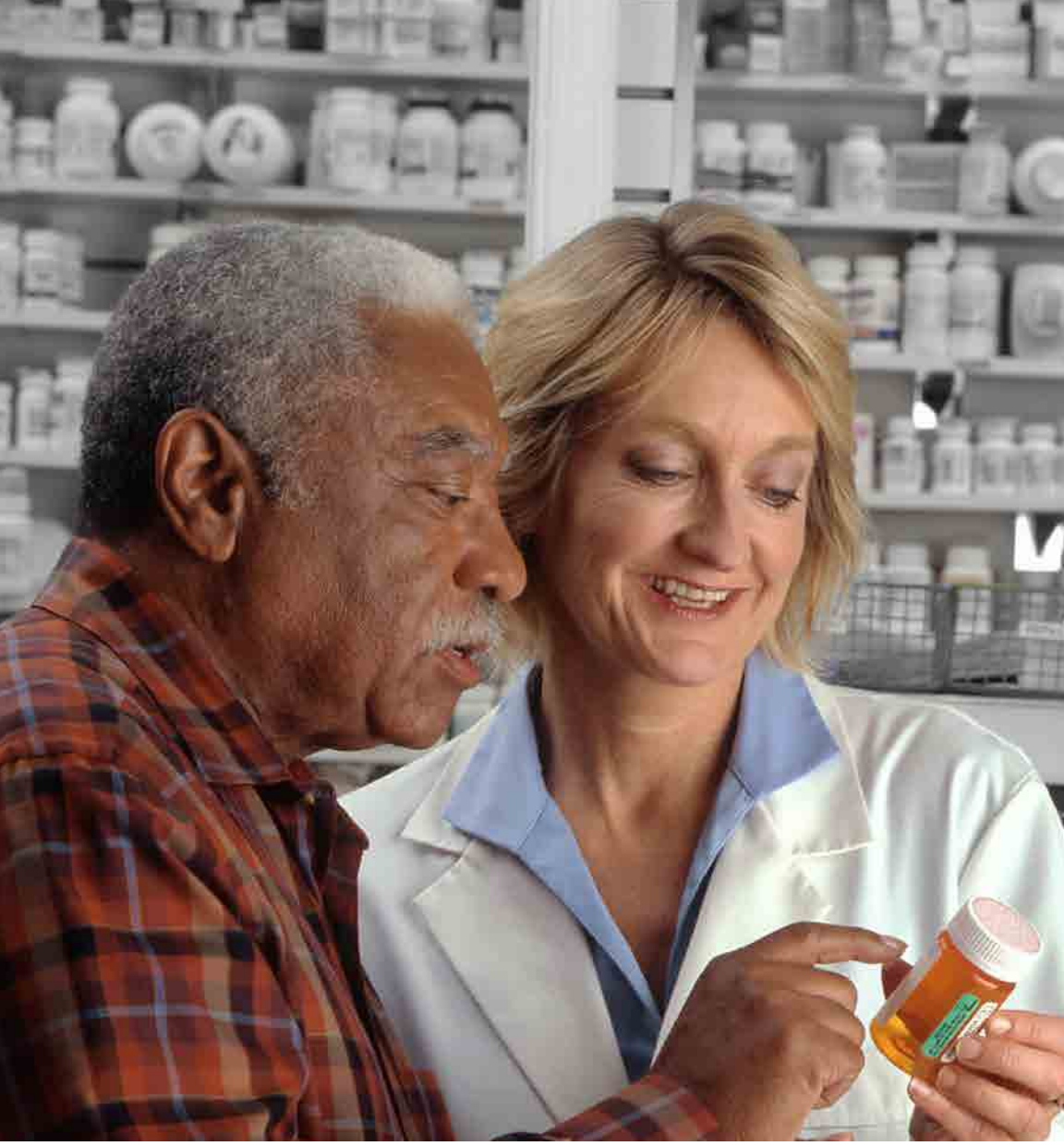

MEDICATIONS TO TREAT PARKINSON'S DISEASE

Parkinson Canada

Blake Bell, was diagnosed with early on-set Parkinson disease at age 50. Now, 59 he lives in Toronto with his wife and son.

This booklet was developed to provide healthcare professionals a concise, yet comprehensive overview of medications to treat people with Parkinson's disease.

It provides a brief description of the pharmacological action of drugs as well as dosing recommendations, an overview of the most common and relevant adverse effects, potential interactions with foods or other drugs, and other practical information to treat people with PD. This booklet also provides tools to help patients track dosing of medications and adverse effects as well resources for clinicians, such as the Non-motor symptoms questionnaire.

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Contents

Brief introduction to Parkinson's disease

Pathophysiology

Parkinson's disease (PD) is the most common movement disorder. About 85% of patients diagnosed with PD are older than 65, and within this age group 1% to 2% have the disorder. [1] PD is a chronic progressive neurological disorder caused by extensive loss of dopaminergic neurons in the pars compacta of the substantia nigra, which results in a loss of dopamine production. As dopaminergic neurons degenerate over time, several compensatory mechanisms delay the onset of motor symptoms until >60% are lost. However, as the number of dopaminergic neurons continues to decline the highly recognizable motor symptoms of PD appear. [2–4]

PD also produces non-motor symptoms. The dorsal motor nucleus and olfactory regions, cholinergic neurons of the nucleus basalis of Meynert, norepinephrine neurons of locus coeruleus, serotonin neurons of the midline raphe and neurons in the cerebral cortex, brainstem, spinal cord and peripheral autonomic nervous system are also involved in PD's pathology, which give rise to non-motor symptoms. [2–5] Examples of these symptoms include loss of smell, depression and anxiety, autonomic dysfunction and cognitive effects, among others. [6]

Clinical presentation

Early motor presentation of PD is characterized by bradykinesia, unilateral or asymmetric resting tremor, and rigidity. A person who presents with two of these three characteristics likely has PD. However, the most widely accepted diagnostic criterion for PD requires that a person with bradykinesia have at least one of the following: muscular rigidity, resting tremor and postural instability. [7] PD is less likely if the following are present: early postural instability (not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction), autonomic dysfunction (characterized by urinary dysfunction/incontinence, fecal incontinence, urinary retention requiring catheterization, persistent erectile failure or orthostatic hypotension), early and prominent

dementia, impaired eye movements, rapid progression and poor response to dopaminergic therapy. In particular, atypical Parkinsonism should be investigated if patients present with the following clinical features within the first three years of diagnosis: falls at presentation and early in the disease course, poor response to levodopa, symmetrical presentation at onset of motor symptoms, rapid progression and autonomic dysfunction. [8]

Many persons with PD will present with non-motor symptoms. [9] Hyposmia, fatigue, depression, constipation and rapid eye movement sleep behaviour disorder may present several years before motor symptoms are evident, while psychiatric disturbances, sialorrhea, urinary urgency, sexual dysfunction and cognitive impairment are late symptoms. [6,9–11]

Drug-induced Parkinson's disease

Several medications may cause presentation of Parkisonian symptoms, worsen the control of PD or unmask PD. Drugs or pharmacological classes commonly associated with drug-induced PD include first- and second-generation antipsychotics, centrally acting dopamine-blocking antiemetics, some cardiovascular medications, among others (*see Table 1*). [12,13] In some individuals, discontinuation of the offending agent can resolve Parkinsonian symptoms, though it may take several months. [12,13]

Table 1: ***Medications that may worsen symptoms of PD or cause drug-induced Parkinsonism*** *[12,13,14]*

Medical purpose	Medications to avoid (higher risk)	Safer alternatives (lower risk)
Antipsychotics	**First-generation antipsychotics** (chlorpromazine, thioridazine, haloperidol) **Second-generation antipsychotics** (risperidone, olanzapine, ziprasidone, aripiprazole)	Quetiapine Clozapine
Nausea drugs/ GI motility agents	Prochlorperazine metoclopramide, promethazine, droperidol	Domperidone, trimethobenzamide, ondansetron, dolasetron, granisetron
Calcium channel blockers	Flunarizine	Diltiazem, verapmil
Antiepileptic agents	Lithium Valproic acid	Phenytoin

Pharmacotherapy for Parkinson's disease

Approach to initiating pharmacological treatment

The decision to initiate drug therapy and the choice of drug to treat PD must be individualized based on patient age, severity of presenting symptoms, co-morbidities, functional impairment, patient employment and patient preference. [6,8] Some patients may opt to delay starting medications if functional impairment from PD is not present. The Canadian Guidelines on Parkinson's Disease should be utilized to guide the initiation of treatment for management of the symptoms of Parkinson's disease.

Medications from six pharmacological classes are commonly used to treat the motor symptoms of PD. These include anticholinergic agents, catechol-amine-O-methyl transferase (COMT) inhibitors, dopamine agonists, dopamine precursors, monoamine oxidase inhibitors, and N-methyl-D-aspartate (NMDA) antagonists.

All of these classes may be initiated as monotherapy at the early stage; however, the choice of the agent will depend on patient age, clinical presentation and severity of symptoms, as well as the history of clinical effects, both benefit and adverse effects, of previously tried medications. Although anticholinergic agents (e.g., benztropine, trihexyphenydyl) are used for controlling tremor, they have limited efficacy and should not be considered first-choice drugs. Use of these agents is typically limited to younger patients with PD because of its high risk for adverse effects, such as confusion and memory impairment, among the elderly. [6,8] Similarly, non-ergot dopamine agonists (e.g., pramipexole and ropinirole) are preferred to ergot-derived dopamine agonists (e.g., bromocriptine) because of adverse effects such as serosal membrane fibrosis and erythromelalgia. [8] Although dosing recommendations are provided for all pharmacological classes used to treat PD, the previously mentioned factors must also be considered when starting pharmacotherapy.

I. Anticholinergic agents

AVAILABLE IN CANADA

Mechanism of action

Postulated to correct an imbalance between dopamine and acetylcholine that occurs in PD, although the mechanism has not been elucidated completely.

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Benztropine (Cogentin)	Tablets, liquid	**Starting dose:** 0.5 mg daily; may increase every 5 days **Usual dose:** 1 – 2 mg twice daily **Maximum dose:** 2 mg three times daily	• Blurred vision • Dry mouth • Constipation • Urinary retention • Sedation • Confusion • Hallucination • Memory loss • Dizziness • Orthostatic hypotension • **Rare:** agitation, nervousness, increase in body temperature (fever or heat stroke)	• Anticholinergic agents are not agents of first choice in the treatment of PD • Modest benefit for the tremor-predominant presentation of PD • Use generally limited to younger persons as adverse effects may be problematic for older persons • Counteracts benefits of cholinesterase inhibitors (donepezil, rivastigmine and galantamine) used to treat cognitive disorders • Increases the anticholinergic side effects when used with other anticholinergic drugs (e.g., urinary antispasmodics, tricyclic antidepressants, etc.)
Trihexyphenidyl (Artane)	Tablets, syrup	**Starting dose:** 1 mg daily at bedtime; may increase every 5 days **Usual dose:** 5mg twice daily or 2mg three times daily **Maximum dose:** 5mg three times daily		
Procyclidine (Kenadrin)	Tablets, syrup 2.5 mg or 5 mg tablet 2.5 mg/5 mL syrup	**Starting dose:** 2.5 mg two - three times daily; increase every 5 days **Usual dose:** 2.5 – 5mg three times daily **Maximum dose:** 5mg four times daily		

II. Catechol-o-methyl transferase (COMT) inhibitors

Mechanism of action

Catechol-o-methyl-transferase (COMT) inhibitors slow or prevent the breakdown of levodopa in peripheral tissues, allowing more levodopa to be available in the brain to be converted to dopamine.

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Entacapone (Comtan)	200 mg tablets **DO NOT CRUSH**	**Starting dose:** 100 - 200 mg with each levodopa dose **Usual dose:** 200mg three – four times daily **Maximum dose:** 1600mg daily	• Profuse diarrhea (can be delayed) • Dyskinesia • Urine discoloration (brown-orange) • Orange stain to teeth if tablets are bitten • Nausea • Changes in liver function • Syncope • Behaviour changes (such as aggression) • Hallucinations	• COMT inhibitor is useful only when given with levodopa to reduce motor fluctuation or "wearing off" • To avoid dyskinesia or psychosis reduce dose by 20% when entacapone is started • Alternatively, add entacapone gradually to one or two of the levodopa doses based on when "wearing off" symptoms typically occur [15] • Advise patients to refrain from taking multiple Stalevo tablets together since only 200 mg entacapone can be taken at one time • Because of increased risk of liver damage with tolcapone, entacapone is the first choice
Entacapone + Levodopa + Carbidopa (Stalevo)	Tablets in combination with levodopa 50 mg, 75 mg, 100 mg, 125 mg, 150 mg (along with carbidopa in 4:1 ratio) **DO NOT CRUSH**	**See levodopa and entacapone**		

II. Catechol-o-methyl transferase (COMT) inhibitors (continued)

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Tolcapone (Tasmar) *(Limited use due to severe risk of liver damage. Available only through Health Canada's Special Access Programme)*	Tablets	**Starting dose:** 100 mg three times daily **Usual dose:** 100 - 200mg three times daily **Maximum dose:** 200mg three times daily	• Orthostatic hypotension • Somnolence • Sleep disorder • Hallucinations • Excessive dreaming • Headache • Confusion • Anorexia • Hepatotoxicity • Dyskinesia • Dystonia • Muscle cramps	

III. Dopamine agonists (DA)

AVAILABLE IN CANADA

Mechanism of action

Dopamine receptor agonists are synthetic agents that simulate dopamine's action in the brain.

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Bromocriptine (Parlodel)	Capsules, tablets	**Starting dose:** 1.25 mg twice daily; increase every 1 – 2 weeks **Usual dose:** 5 – 10mg three times daily **Maximum dose:** 10mg three times daily	• Dizziness • Fatigue • Headache • Blurred vision • Constipation • Weakness • Rhinitis • Serious pulmonary and cardiac valve fibrosis	• Bromocriptine is an ergot derivative and should not be considered as the dopamine agonist of first choice • Slow dose titration to minimize nausea and dizziness • Indicated as monotherapy for early PD or as an adjunct to levodopa in advanced PD • Non-ergot DAs — pramipexole, ropinirole, and rotigotine patch preferred to ergot DA such as bromocriptine because of risk of serious pulmonary or cardiac valve fibrosis • Avoid rotigotine patch if patient has sulfite allergy (more common in patients with asthma)
Pramipexole (Mirapex)	Tablets 0.125mg, 0.25mg, 0.5mg, 1mg and 1.5mg	**Starting dose:** 0.125 mg three times daily; twice daily if CrCL 35–59 mL/min; once daily if CrCL < 35 mL/min; increase every 7 days **Usual dose:** 0.5 – 1.5mg three times daily **Maximum dose:** 1.5mg three times daily	• Orthostatic hypotension • Severe drowsiness may affect driving ability • Psychosis • Hallucinations • Impulse control disorders (ICDs) • Leg edema	

III. Dopamine agonists (DA) (continued)

AVAILABLE IN CANADA

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Ropinirole (Requip)	Tablet 0.25 mg, 1 mg, 2 mg and 5 mg	**Starting dose:** 0.25 mg three times daily; increase every 7 days **Usual dose:** 1 – 5mg three times daily **Maximum dose:** 8 mg three times daily	• Orthostatic hypotension • Severe drowsiness may affect driving ability • Psychosis • Hallucinations • Impulse control disorders (ICDs) • Leg edema	• Bromocriptine is an ergot derivative and should not be considered as the dopamine agonist of first choice • Slow dose titration to minimize nausea and dizziness • Indicated as monotherapy for early PD or as an adjunct to levodopa in advanced PD • Non-ergot DAs — pramipexole, ropinirole, and rotigotine patch preferred to ergot DA such as bromocriptine because of risk of serious pulmonary or cardiac valve fibrosis • Avoid rotigotine patch if patient has sulfite allergy (more common in patients with asthma) • Rotate application site to prevent skin irritation (Ritigotine only)
Rotigotine (Neupro)	Patch 1 mg, 2 mg, 3 mg, 4 mg, 6 mg and 8 mg	**Starting dose:** 2mg patch once daily; increase by 2mg/24 hours every 7 days **Maximum dose:** 16mg per 24 hours		

Additional notes about dopamine agonists

Impulse control disorders

Dopamine agonists may cause impulse control disorders (ICDs). [16] ICDs are evident when individuals cannot resist behaving in ways that can have negative psychosocial consequences. Symptoms include any uncontrolled or compulsive behaviours, such as uncontrolled eating, shopping, gambling and sexual urges. Although the literature reports that about 14% of patients treated with DAs develop ICDs, in clinical practice the percentage can be much higher. Patients most at risk are younger individuals, men more so than women, with a known or family history of addiction or mood disorder. [16]

ICDs can lead to significant financial and social disruption, but are usually reversible with dose reduction or discontinuation. Patients and family members should be instructed to watch for ICDs before starting DA treatment. [17] The Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease–Rating Scale (QUIP–RS) screens for compulsive gambling, sex, buying, eating, hobbyism, punding and intentional over medication. [18]

Dopamine-agonist withdrawal syndrome

Withdrawal symptoms are more common in patients with ICDs. Symptoms include anxiety, panic attacks,
dysphoria, diaphoresis, pain, orthostatic hypotension, and drug cravings. [19] Medication management involves a slower withdrawal.

Adverse effects

The adverse effects of dopamine agonists are generally similar to those associated with levodopa. However, certain side effects, such as excessive daytime sleepiness, visual hallucinations, confusion and swelling of the legs, occur more commonly with use of dopamine agonists than with levodopa. When using DAs, older adults with PD are more likely than younger people to have troublesome adverse effects such as confusion, hallucination, leg edema and dizziness. [20]

IV. Levodopa (Dopamine precursor)

Mechanism of action

Dopamine cannot cross the blood–brain barrier. When administered peripherally, it will produce adverse effects, such as nausea and dizziness, but will not be effective in controlling symptoms of PD. Levodopa is a dopamine precursor that can cross the blood–brain barrier, but it is rapidly broken down in the body before it crosses the blood brain barrier so large doses are needed to produce an effect on motor symptoms of PD. Dopa-decarboxylase inhibitors (benserazide and carbidopa) are given concurrently with levodopa to prevent its breakdown in the periphery, allowing levodopa to cross the blood–brain barrier.

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Levodopa + Carbidopa Immediate Release (IR) Sinemet	Tablet, 100/10, 250/25 100/25 (higher carbidopa ratio is preferred)	**Starting dose:** ½ tablet of 100/25 twice daily to three times daily with non-protein snack **Usual dose:** 100/25 three to four times daily to 250/25mg three times daily **Maximum dose:** > 2g daily **May crush and take with carbonated drink to speed onset**	• Hallucinations • Nausea • Confusion • Dizziness • Vivid dreams • Fatigue	• Protein or iron ↓ bioavailability • Titrate slowly to prevent nausea and dizziness • Constipation and anticholinergics agents ↓ GI motility and delay onset • Antacid, iron, protein food ↓ absorption • Hypotension from Levodopa + antihypertensive agents • Controlled-release formulations are rarely used during the day because of delayed and unpredictable onset • Bioavailability of sustained release formulation is about 70% of immediate release • **Very rare:** Risk of neuroleptic malignant syndrome if stopped abruptly

IV. Levodopa (Dopamine precursor) (continued)

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Levodopa+ Benserazide Prolopa	Capsules 50/12.5, 100/25, 200/50	**Starting dose:** 50/12.5mg twice daily; increase every 3 – 7 days **Usual dose:** 100/25mg three to four times daily to 200/50mg three times daily **Maximum dose:** > 2g daily	• Hallucinations • Nausea • Confusion • Dizziness • Vivid dreams • Fatigue	• Protein or iron ↓ bioavailability • Titrate slowly to prevent nausea and dizziness • Constipation and anticholinergics agents ↓ GI motility and delay onset • Antacid, iron, protein food ↓ absorption • Hypotension from Levodopa + antihypertensive agents • Controlled-release formulations are rarely used during the day because of delayed and unpredictable onset • Bioavailability of sustained release formulation is about 70% of immediate release • **Very rare:** Risk of neuroleptic malignant syndrome if stopped abruptly
Levodopa Carbidopa Controlled Release (CR) Sinemet CR	Tablets 100/25, 200/50 **DO NOT CRUSH**	1 tablet of 100/25mg or 200/50mg at bedtime daily to prevent symptoms at night or morning wearing off		
Levodopa+ Carbidopa Duodopa	Intestinal gel 5 mg/mL	40–120 mg/hour for 16 hours		• DUODOPA® should be prescribed only by neurologists who are experienced in treating patients with PD, and who have completed the DUODOPA® education program that includes training in the criteria for selecting suitable patients; initiation and management with DUODOPA® therapy via naso-intestinal infusion and percutaneous endoscopic gastrostomy; postprocedural care; and, the risks associated with the procedure and long-term use of the PEG-J. • The use of Duodopa gel, delivered via a J-tube continuously to the intestines, may be used to produce stable levels of levodopa throughout the day to reduce the motor fluctuation of wearing off and dyskinesia.

V. MAO-B inhibitors

Mechanism of action

These drugs prevent the metabolism of dopamine in the brain by inhibiting the action of the enzyme monoamine oxidase B (MAO-B). This results in increased amounts of dopamine in the brain.

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Rasagiline Azilect	Tablets 0.5 mg, 1 mg	**Starting dose:** 0.5 mg daily **Usual dose:** 1mg daily **Maximum dose:** 1 mg daily	• Intense dreams • Dizziness • Insomnia • Weight loss • Constipation	• Monoamine oxidase B inhibitors may exacerbate the potential adverse effects of nausea and dizziness associated with the use of other dopinamergic medications such as levodopa and dopamine agonists.
Selegiline	Capsules 50/12.5, 100/25, 200/50 50/12.5 bid to tid	**Starting dose:** 2.5–5 mg qam and noon **Usual dose:** 5mg two times daily **Maximum dose:** 5mg twice daily	• Selegiline can cause insomnia if taken later in the day and should be taken before noon	

VI. NMDA Antagonist

Mechanism of action

TGlutamate (NMDA) receptor antagonist that reduces dyskinesia. Has mild anti-Parkinsonian action in addition.

Generic names (Brand names)	Formulations available	Common starting, usual and maximum doses	Adverse effects	Comments
Amantadine Symmetrel	100mg capsules 50mg/5mg syrup	**Starting dose:** 100 mg once daily; increase every 7 days **Usual dose:** 100mg twice to three times daily **Maximum dose:** 200mg twice daily **Reduce dose if renal dysfunction**	• Dizziness • Insomnia if taken late in the day • Confusion • Hallucinations • Peripheral edema • Constipation • Urinary retention • Livedo reticularis (red-purple discolouration of the skin); occurs in < 1%)	• Reduce dose of amantadine if patient has decreased creatinine clearance.

Notes on prescribing and monitoring Parkinson's medications

1. Start with low doses and gradually increase if needed.
2. Have patients keep a medication/mobility diary to record when they take their medication and when they experience adverse effects or wearing off, to guide dosing adjustments.
3. Encourage the use of compliance packaging (e.g., blister packs, pill boxes, dosette) and multiple alarms (e.g., clock alarms and smart phone alarms) to help patients remember to take their medications on time.
4. Assess patients' ability to swallow, as this can be impaired by PD. Some medications cannot be crushed. If required, levodopa suspension can be prepared.
5. Dietary protein competes with levodopa for absorption and onset of action may be delayed after a meal. If patients complain of delayed onset or variability in effect, advise patients to take levodopa ½–1 hour before a meal or protein-rich foods such as milk, eggs or peanut butter.
6. To reduce severe nausea, improve gastric motility and to speed levodopa's onset of action, domperidone can be given before each dose. The dose of domperidone should be limited to 30 mg/day because of the potential for an elevated risk of QT interval prolongation.
7. Since all PD medications can cause dizziness, fatigue or drowsiness, patients should be advised to minimize or avoid alcohol.
8. If patient with PD is admitted to a hospital, advise patient and/or caregivers to provide hospital staff with the exact times medications are to be administered so doses are given on the same schedule the patient follows at home, not the hospital's schedule. Provide staff with a list of medications that are contraindicated in PD. Before surgery, patients should take the first dose of PD medication early in the morning with sips of water. If prolonged "npo" is required, rectal levodopa formulation may be required. If patient is on entacapone or Stalevo, educate staff not to be alarmed by patient's orange brown urine.
9. Do not substitute medications used to treat Parkinson's disease.
10. Resume medications immediately following procedures, unless the patient is vomiting or is severely incapacitated.
11. Ambulate as soon as medically safe. Patients may require assistance.

Common interactions with other drugs and food

Parkinson medication (generic name)	Brand name	Interaction (may either increase or decrease the effect of Parkinson medication)
Levodopa-Carbidopa	Sinemet®	Antacids, antipsychotics, metoclopramide, iron, antihypertensives, high protein foods*
Rotigotine	Neupro®	Antipsychotics, metoclopramide
Pramipexole	Mirapex®	Amantadine, cimetidine, diltiazem, quinidine, ranitidine, triamterene, verapmil
Ropinirole (Requip)	Requip®	Ciprofloxacin, clarithromycin, erythromycin, fluvoxamine, itraconazole, propranolol Ropinirole concentrations ↑ when combined with CYP1A2 inhibitor (e.g., ciprofloxacin); monitor and adjust dosage if needed
Benztropine	Congentin®, Kynesia®	Cholinergic agents (e.g. donepezil), antipsychotics
Trihexyphenidyl	Trihexyphenidyl	Cholinergic agents (e.g. donepezil), antipsychotics
Selegiline	Eldepryl®, Carbex®	Amphetamines, bupropion, buspirone, dextromethorphan, methadone, methylphenidate, pseudoephedrine, antidepressants
Rasagiline	Azilect®	Opioids, antidepressants, decongestants CYP1A2 inhibitor (e.g., ciprofloxacin, fluvoxamine) may ↑ rasagiline concentration
Entacapone	Comtan®	Antidepressants
Amantadine	Symmetrel®	Iron

* *High protein foods decrease the absorption of levodopa, making it less effective. It is best for patients to try to maintain a diet with steady amounts of protein.*

Medications used to treat non-motor symptoms of PD in Canada

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Depression and Anxiety	Depression and anxiety are common, reported in up to 50% of patients with PD. They may precede motor symptoms, significantly affect patient's functions and quality of life. Antidepressants are effective. Patient education is crucial to ensure medication adherence. Optimizing medications used to treat both PD and depression/anxiety can improve or resolve both conditions.	
	SSRI	
	Citalopram (Celexa®)	**Dosing:** 10 - 20 mg once daily For all SSRIs, and SNRIs, start with a low dose and titrate slowly. Do not discontinue abruptly but withdraw slowly. • Watch for rare hyponatremia for all SSRIs and SNRIs
	Escitalopram (Cipralex®)	**Dosing:** 5 - 20 mg once daily
	Paroxetine (Paxil®)	**Dosing:** 10 - 40 mg once daily • Generally avoided in older patients because of a higher anticholinergic load
	Fluoxetine (Prozac®)	**Dosing:** 10 - 40 mg daily
	Sertraline (Zoloft®)	**Dosing:** 25 - 100 mg daily
	SNRI	
	Desvenlafaxine (Pristiq®)	**Dosing:** 50 mg daily
	Venlafaxine (Effexor®)	**Dosing:** 25 - 75 mg twice daily
	Duloxetine (Cymbalta®)	**Dosing:** 30 - 60 mg once daily

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Depression and Anxiety	**Tri-cyclic antidepressants (TCAs)** • Taken at night to improve sleep, anxiety and appetite	
	Nortriptyline (Pamelor®)	**Dosing:** 10 - 50 mg at bedtime
	Amitriptyline (Elavil®)	**Dosing:** 10 - 50 mg at bedtime • Generally avoided in older patients because of a higher anticholinergic load
	Imipramine (Tofranil®)	**Dosing:** 10 - 50 mg at bedtime
	Other antidepressants	
	Buproprion (Wellbutrin®)	**Dosing:** 75 - 150 mg once to twice daily • Buproprion + PD medications may increase risk of restlessness, gait disturbances and dizziness because of additive dopamine agonist effect. May lower dose and monitor closely.
	Miscellaneous	
	Mirtazipine (Remeron®)	**Dosing:** 15 - 30 mg at bedtime
Pain	PD may reduce pain thresholds. Morning dystonia and muscle pain/stiffness often occur during off periods, while dyskinesia at peak drug level may also cause pain. Stretching, massage and adjustment of PD drugs are helpful. Acetaminophen instead of oral NSAIDs is safer for chronic pain.	
	Acetaminophen (Tylenol ES® or Arthritis®)	**Effective for mild pain or osteoarthritis** **Max dose:** 3,250 mg/day for long-term use
	Duloxetine (Cymbalta®)	**Initial dose:** 30 mg once daily
	Gabapentin (Neurontin®)	**Initial dose:** 100 mg twice to three times daily **Watch for sedation and leg edema**
	Pregabalin (Lyrica®)	**Initial dose:** 25 mg twice daily **Watch for sedation and leg edema**

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Drooling	**Glycopyrrolate** (Robinul)	**Dosing:** 1 - 2mg two to three times daily as needed
	Atropine solution (Isopto Atropine®) **Ipratropium bromide** (Atrovent nasal spray®)	**Apply 1 drop/spray under the tongue bid prn** **Watch for anticholinergic side effects**
	Scopolamine (Buscopan®)	**consult with specialist**
	Botulinum Toxin A (Botox®/Xeomin®)	**consult with specialist**
Nausea and vomiting	**Domperidone** (Motilium®)	**Max:** 10 mg twice to three times daily before levodopa **Watch for QT prolongation especially with drugs with similar concern**
	Ondansetron	**4mg three times daily as needed**
Bladder dysfunction	**i. Overactive bladder**	
	Tolterodine (Detrol LA®)	**4 mg at bedtime**
	Solifenacin (Vesicare®)	**5 mg at bedtime**
	Darifenacin (Enablex®)	**7.5 mg at bedtime**

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Bladder dysfunction	**ii. Nocturia**	
	Trospium Chloride (Trosec®)	**20 mg at bedtime**
	Desmopressin (Nocdurna®)	**25–50 µg SL at bedtime. Monitor serum sodium within 4–8 days and in 1 month to prevent hyponatremia.** **Not recommended if CrCL < 50 mL/min or history of SIADH, cardiac insufficiency**
	iii. Urinary retention	
	Bethanechol chloride (Duvoid®)	**10–25 mg twice to three times daily**
PD dementia (↑ with age and PD duration)	**Cholinesterase inhibitors**	**May improve apathy, behavioural disturbances and hallucination** **Not recommended if heart block, syncopes or significant bradycardia. Monitor ECG.** **Require slow dose titration**
	Rivastigmine (Exelon®) oral and patch	**Oral:** 1.5 - 3mg twice daily with food **Patch:** 4.5 - 9.6mg patch once daily
	Donepezil (Aricept®)	**2.5–5 mg once daily with food. (Give in the morning if patient experiences vivid dreams)**
	Galantamine (Reminyl ER®)	**8 mg once daily with food**
	NMDA receptor antagonist	
	Memantine (Ebixa®)	**Start with 5 mg every morning, titrate to 10 mg twice daily. (Max: 10 mg/day if severe renal impairment)**

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Visual hallucinations Occurs in later stages and in those with cognitive decline	**1**. Rule out medical causes of delirium **2**. Taper or stop sedative, anxiolytic and anticholinergic therapy **3**. Discontinue PD medications according to the following order to minimize risk of worsening PD (slow taper may be required): anticholinergics, amantadine, MAO-B inhibitor, dopamine agonist, entacapone, levodopa **4**. Antipsychotic agents decrease dopamine and serotonin, which are involved in hallucinations. Use lowest dose to avoid sedation and low blood pressure. Avoid haloperidol and other atypical antipsychotics (risperidone or olanzapine).	
	Clozapine (Clozaril®)	**Initial dose:** 12.5–25 mg at bedtime. Requires regular blood monitoring due to life-threatening agranulocytosis (0.38%). **Register with CLOZAIL registry**
	Quetiapine (Seroquel®)	**Initial dose:** 12.5–25 mg at bedtime **No blood test required.**
Apathy	**Methyphenidate** (Biphentin, Concerta®, Ritalin®)	**5 - 15 mg twice to three times daily**
Erectile dysfunction	**Sildenafil** (Viagara®)	**Dose before intercourse:** 50–100 mg
	Vardenafil (Levitra®)	**Dose before intercourse:** 5–10 mg
	Tadalafil (Cialis®)	**Dose before intercourse:** 10–20 mg

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Orthostatic hypotension	Orthostatic drop in SBP of ≥20 mmHg or drop in DBP of ≥10 mmHg within 3 min of standing up. Attempt the following before initiating treatment: • Reassess antihypertensive agents • If it occurs after a meal, avoid large meals and alcohol • ↑ salt intake and avoid straining stool	
	Pyridostigmine bromide (Mestinon®)	**30–60 mg four times daily, may increase drooling and urinary frequency**
	Midodrine (Amatine®)	**Initial dose:** 2.5 mg twice daily **last dose should be given no later than mid-afternoon to prevent supine hypertension at night**
	Fludocortisone (Florinef®)	**Dosing:** 0.05–0.1 mg daily. Watch for pedal edema or hypokalemia
	Desmopression	**High risk of supine hypertension at doses of 100–400 µg QHS; therefore, not a drug of choice.**
Insomnia	Etiology is multifactorial: pain, tremor, stiffness, medication side effects, anxiety, nocturia, restless leg syndrome. Identify and manage underlying treatable cause	
	Doxepin (Silenor®)	**Works on receptor for sleep maintenance** **Initial dose:** 3 mg at bedtime
	Melatonin	**1–2 mg SL to help sleep initiation** **5 mg time release formulation to sustain sleep**

Non-motor symptoms	Generic name (brand name)	Initial dose and comment
Insomnia	**Trazodone** (Desyrel®)	**25–50 mg at bedtime** **Trazodone can increase the risk of hypotension and falls in the older adult**
	Mirtazipine (Remeron®)	**15 - 30 mg at bedtime**
	Zopiclone (Imovane®)	**Benzodiazepine receptor analogue** **Initial dose:** 5 mg at bedtime **Not a drug of choice as increases the risk of falls and cognitive impairment**
Excessive daytime sleepiness	**Methylphenidate** (Biphentin®, Concerta®, Ritalin®)	**5 - 15 mg twice to three times daily**
	Modafinil (Alertec®) *trial of caffeine and rule out sleep apnea first*	**Initial dose:** 100–200 mg every morning **Long-term use may ↑ cardiovascular side effects, anxiety**
Restless leg syndrome (RLS)	**Iron deficiency (with low ferritin) causes RLS**	**Ferrous sulfate, ferrous gluconate, ferrous fumarate 300 mg once daily**
	Pramipexole (Mirapex®)	**0.125–0.5 mg at bedtime**
	Pregabalin (Lyrica®)	**Start with 50 mg at bedtime and slowly titrate up**
	Gabapentin (Neurontin®)	**100–300 mg at bedtime**

Glossary

Dyskinesia: Involuntary or unusual movements, such as jerking, twitches or spasms. They can affect any part of the body. Dyskinesias can vary from mild to severe. Dyskinesia occurs because of a combination of PD and medications taken to treat PD. It is most common in people who have been taking levodopa for many years. The prescription often has to be adjusted to find a balance between enough medication to control the symptoms, and a dose that does not bring on too much dyskinesia.

"On/Off": Describes changes in the ability to move, which happens in some people with long-standing Parkinson's who take levodopa. In the 'on' state, the person can move, while in the 'off' state, they can stop moving altogether. People can switch from one state to the other in minutes or even seconds.

"Wearing-off": An effect experienced by many people who have been taking PD drugs for some time. The dose does not work as long as it used to and the beneficial effects of the drug wear off before it is time to take the next dose.

PD NMS QUESTIONNAIRE

Name: ..... Date: ..... Age: .....

Male ☐ Female ☐

NON-MOVEMENT PROBLEMS IN PARKINSON'S

The movement symptoms of Parkinson's are well known. However, other problems can sometimes occur as part of the condition or its treatment. It is important that the doctor knows about these, particularly if they are troublesome for you.

A range of problems is listed below. Please tick the box 'Yes' if you have experienced it **during the past month.** The doctor or nurse may ask you some questions to help decide. If you have **not** experienced the problem in the past month tick the 'No' box. You should answer 'No' even if you have had the problem in the past but not in the past month.

Have you experienced any of the following in the last month?

	Yes	No
1. Dribbling of saliva during the daytime	☐	☐
2. Loss or change in your ability to taste or smell	☐	☐
3. Difficulty swallowing food or drink or problems with choking	☐	☐
4. Vomiting or feelings of sickness (nausea)	☐	☐
5. Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (faeces)	☐	☐
6. Bowel (fecal) incontinence	☐	☐
7. Feeling that your bowel emptying is incomplete after having been to the toilet	☐	☐
8. A sense of urgency to pass urine makes you rush to the toilet	☐	☐
9. Getting up regularly at night to pass urine	☐	☐
10. Unexplained pains (not due to known conditions such as arthritis)	☐	☐
11. Unexplained change in weight (not due to change in diet)	☐	☐
12. Problems remembering things that have happened recently or forgetting to do things	☐	☐
13. Loss of interest in what is happening around you or doing things	☐	☐
14. Seeing or hearing things that you know or are told are not there	☐	☐
15. Difficulty concentrating or staying focussed	☐	☐
16. Feeling sad, 'low' or 'blue'	☐	☐
17. Feeling anxious, frightened or panicky	☐	☐
18. Feeling less interested in sex or more interested in sex	☐	☐
19. Finding it difficult to have sex when you try	☐	☐
20. Feeling light headed, dizzy or weak standing from sitting or lying	☐	☐
21. Falling	☐	☐
22. Finding it difficult to stay awake during activities such as working, driving or eating	☐	☐
23. Difficulty getting to sleep at night or staying asleep at night	☐	☐
24. Intense, vivid dreams or frightening dreams	☐	☐
25. Talking or moving about in your sleep as if you are 'acting' out a dream	☐	☐
26. Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move	☐	☐
27. Swelling of your legs	☐	☐
28. Excessive sweating	☐	☐
29. Double vision	☐	☐
30. Believing things are happening to you that other people say are not true	☐	☐

All the information you supply through this form will be treated with confidence and will only be used for the purpose for which it has been collected. Information supplied will be used for monitoring purposes. Your personal data will be processed and held in accordance with the Data Protection Act 1998.

Developed and validated by the International PD Non Motor Group
For information contact: susanne.tluk@uhl.nhs.uk or alison.forbes@uhl.nhs.uk

To download and print additional full size copies of this tool, visit www.parkinson.ca.

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PARKINSON DAILY DIARY

http://www.cmdg.org/MDC_tools/PDDIARY/pddiary.htm

Name: _____

Date: _____

Instructions: This is a tool to track response to medication and will be used to adjust the doses and timing of medications. Please place only one checkmark under each time of day column in the row that best describes the patient's motor state over the 1-hour period before the time indicated (i.e., in the 7:00 a.m. column indicate the average motor state from 6:00 to 7:00 a.m. or if asleep check only the asleep row.

Motor State – Time of Day	"ON" with Dyskinesia Too Much Movement	"ON" Normal Movement	"OFF" Too stiff and slow	Asleep	PD Medication Time
6:00 a.m.					
7:00 a.m.					
8:00 a.m.					
9:00 a.m.					
10:00 a.m.					
11:00 a.m.					
Noon					
1:00 p.m.					
2:00 p.m.					
3:00 p.m.					
4:00 p.m.					
5:00 p.m.					
6:00 p.m.					
7:00 p.m.					
8:00 p.m.					
9:00 p.m.					
10:00 a.m.					
11:00 a.m.					
Midnight					

A Parkinson's Prescription for You

I recommend that you contact Parkinson Canada to discuss and understand your diagnosis and prognosis.

You, your family or caregiver will have many questions and there are answers available. Take that first step by calling **1-800-565-3000** today.

Experienced personnel will listen and treat you with respect and confidentiality. You will receive helpful information and learn about community resources that may improve your quality of life. Email **info@parkinson.ca** to get started.

Visit **www.parkinson.ca** to learn about living well with Parkinson's.

Referred by: _____ Date: _____/_____/_____

Parkinson Canada

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