PARKINSON’S DISEASE: NON-MOTOR SYMPTOM MANAGEMENT

Non-motor symptoms can have a large impact on quality of life and level of functioning in patients with PD. In some patients, their non-motor symptoms are more problematic than their motor symptoms. Please note that in the table below, many of the medications may have been studied in clinical trials and can be recommended based on efficacy in these trials (and therefore would be considered evidence-based) but are not FDA-approved for use in Parkinson’s disease. FDA approval requires studies to show benefit as well as an extensive and costly application process, typically by the pharmaceutical company. The use of medications for conditions beyond what has been FDA approved for is called off label and this is noted below.

### FATIGUE

- Very common in PD, sometimes improved when motor symptoms are improved
- May be related to muscle fatigue, sleep deprivation, depression, or even the meds of PD itself
- Could manifest as apathy (the lack of will to do things)

<table>
<thead>
<tr>
<th>Potential testing</th>
<th>Non-medication treatment</th>
<th>Medication options</th>
<th>Potential side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Blood test for thyroid, anemia and testosterone levels</td>
<td>• Get regular sleep</td>
<td>• Rasagiline 1 mg (Azilect)</td>
<td>• Methylphenidate may be habit-forming. Both medications could cause agitation, exacerbation of hallucinations, delusions, insomnia, headache</td>
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<tr>
<td>• Consideration of poor quality / quantity of sleep</td>
<td>• Exercise</td>
<td>Off label options:</td>
<td>• Azilect can cause dizziness, nausea, headache, indigestion, agitation, back pain, dyspepsia; may aggravate dyskinesias</td>
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<tr>
<td>• Evaluation for underlying depression</td>
<td>• Eat a balanced diet</td>
<td>• Modafinil (Provigil) for excessive daytime somnolence</td>
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<td></td>
<td></td>
<td>• Methylphenidate (Ritalin)</td>
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### CONSTIPATION

- Due to changes in the activity of the autonomic nervous system which controls the visceral organs
- Constipation due to slowing of the gut's wave-like movements, known as slow transit constipation

<table>
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<th>Things to know</th>
<th>Potential testing</th>
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<tr>
<td>• Bulking agents such as fiber are less effective because the gut does not respond well from a neurological perspective</td>
<td>• Often none is required</td>
<td>• Increase fiber in the diet</td>
<td>Over the counter:</td>
<td>• Diarrhea, abdominal pain, bloating</td>
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<tr>
<td>• It’s important to treat constipation aggressively to prevent hemorrhoids, diverticulosis, anal fissures, rectal prolapse, fecal impaction</td>
<td>• Consultation with a gastroenterologist</td>
<td>• Increase physical activity</td>
<td>• Senna (SennaKot), a natural stimulant laxative</td>
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<td></td>
<td>• Sigmoidoscopy or colonoscopy to exclude a structural blockage</td>
<td>• Reduce medications that can cause constipation</td>
<td>• Miralax (polyethylene glycol) 1 capful daily</td>
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<td></td>
<td>• Colon transit studies</td>
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<td>• Colace (stool softener)</td>
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<td></td>
<td></td>
<td></td>
<td>• Dulcolax (laxative)</td>
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<td></td>
<td></td>
<td></td>
<td>• Magnesium citrate</td>
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<td></td>
<td>• Lactulose</td>
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<td>Prescription / off label:</td>
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<td></td>
<td>• Linzess reduces transit time and decreases visceral pain</td>
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### Orthostatic Hypotension (OH)

- Lightheadedness upon standing due to drops in blood pressure (BP)
- Due to changes in the activity of the autonomic nervous system which controls the visceral organs

#### Things to know
- Patients with OH may also have supine hypertension, meaning their blood pressure is very high lying down. Treating OH may exacerbate supine hypertension and vice versa
- Patients may need to sleep with the head of bed at 30 degrees, as well as using a short-acting BP med at night plus an OH med during the day

#### Potential testing
- Check BP and pulse lying down, sitting, then standing in clinic
- Keep a BP log, checked in lying down, sitting and standing positions on a daily basis

#### Non-medication treatment
- Keep out of bed during the day
- Wear compression stockings (knee high or thigh high)
- Wear an abdominal binder
- Stay hydrated, increase salt in the diet
- Increase exercise
- Isometric exercises in the legs and arms prior to standing up

#### Medication options

**Prescription:**
- Droxidopa (Northera) 100 mg 3 times daily up to 600 mg 3 times daily
- Midodrine up to 10 mg 3 times daily

**Off label:**
- Fludricortisone (Florinef) up to 0.3 mg daily
- Pyridostigmine (Mestinon) 60 mg 3 times per day

#### Potential side effects
- Supine hypertension is often asymptomatic but can be very dangerous and can cause stroke, heart attack, retinal damage, kidney damage
- Other side effects of midodrine include tingling, itching, burning while urinating; of pyridostigmine include abdominal pain, urinary frequency, tearing, sweating
- Pyridostigmine can exacerbate tremor and rigidity

### Urinary Symptoms

- Frequency (too often)
- Urgency (can’t hold it as long)
- Incontinence (accidents)
- Nocturia (waking up several times at night to urinate)
- Urinary retention (bladder cannot empty)

#### Things to know
- Due to changes in the activity of the autonomic nervous system which controls the visceral organs, known as autonomic dysfunction

#### Potential testing
- Consultation with a urologist
- For men, checking the prostate
- Urodynamics (checking neurological control of the bladder and sphincter)

#### Non-medication treatment
- Reduce fluid intake prior to bedtime
- Reduce medications that can cause urinary retention
- Avoid alcohol and caffeine
- Bladder retraining
- Improve mobility

#### Medication options

**Overactive Bladder:**
- Tolterodine 2-4 mg / day
- Oxybutynin 5-15 mg / day
- Soifenacin 5-10 mg / day
- Onabotulinum toxin (Botox) injection

**Off label:**
- Urinary retention:
  - Bethanechol 25-75 mg / day
- Nocturia:
  - Desmopressin spray

#### Potential side effects
- Anticholinergic medications for overactive bladder can cause confusion, dry mouth, constipation, urinary retention, blurry vision and redness
- Cholinergic agonist medications such as bethanechol can worsen PD symptoms and cause diarrhea, sweating, nausea, excess saliva
**SEXUAL DYSFUNCTION**
- Reduced libido
- Erectile dysfunction
- Increased libido / hypersexuality can occur with dopamine agonist use

**Things to know**
- Due to changes in the activity of the autonomic nervous system which controls the visceral organs, known as autonomic dysfunction

**Potential testing**
- Consultation with a urologist
- Testosterone levels
- Evaluation for diabetes

**Non-medication treatment**
- Pump devices

**Medication options**
- Sildenafil (Viagra) 50-100 mg prior to sexual activity

**Potential side effects**
- Headache, flushing, dyspepsia, temporary visual symptoms

**THERMOREGULATORY DYSFUNCTION**
- Sweating
- Flushing
- Cold intolerance
- Often associated with peak-dose dyskinesias

**Things to know**
- Due to changes in the activity of the autonomic nervous system which controls the visceral organs, known as autonomic dysfunction

**Potential testing**
- Blood tests for hormonal or metabolic dysfunction

**Non-medication treatment**
- Air conditioning
- Heating systems

**Medication options**
- Trihexyphenidyl 2 mg 3 times per day

**Potential side effects**
- Dry mouth, constipation, urinary retention, confusion, blurry vision, redness

**DROOLING (SIALORRHEA)**
- Due to reduced swallow frequency

**Potential testing**
- Typically none

**Non-medication treatment**
- Use of chewing gum or hard candy to encourage swallowing

**Medication options**
- Off label:
  - Glycopyrrolate 1 mg 3 times per day
  - Onabotulinum toxin (Botox) injection to the submandibular and parotid glands

**Potential side effects**
- For glycopyrrolate, dry mouth, confusion, headache, diarrhea, fatigue
- For onabotulinum toxin (Botox) injection, dry mouth and difficulty swallowing

**DIFFICULTY SWALLOWING (DYSPHAGIA)**
- Coughing after swallowing
- “Silent” aspiration
- Delayed gastric emptying causing early satiety, known as gastroparesis

**Potential testing**
- Swallow study
- Evaluation by a speech therapist
- Consultation with a gastroenterologist
- Gastric emptying study

**Non-medication treatment**
- Chin tuck
- Sit up straight
- Chew thoroughly and swallow slowly
  - Small bites and sips
- Clear the throat with a double swallow and a cough
- Thickening product for thin liquids
- Puree foods

**Medication options**
- For delayed gastric emptying, erythromycin 50-250 mg 3-4 times per day or domperidone 10-20 mg 2-4 times per day

**Potential side effects**
- Nausea, vomiting, abdominal pain; breast leakage from domperidone due to excess prolactin levels
SLEEP SYMPTOMS

- Insomnia (trouble falling or staying asleep)
- Trouble rolling over in bed
- Restless legs syndrome

**Things to know**
- Tremor, rigidity and dystonia could interfere with sleep and therefore a nighttime controlled release levodopa or dopamine agonist may help for sleep
- Depression and anxiety may contribute to insomnia and should be addressed

**Potential testing**
- Sleep study is often indicated to assess for sleep apnea, which can exacerbate sleep issues
- Iron studies for restless legs syndrome

**Non-medication treatment**
- Avoid caffeine and alcohol
- Avoid screen use 2 hours prior to bedtime
- Keep the bedroom dark at nighttime
- Positive airway pressure for sleep apnea

**Medication options**
- Melatonin
- Tryptophan
- Gabapentin or gabapentin enacarbil for restless legs syndrome
- Diphenhydramine

**Potential side effects**
- Benzodiazepines such as temazepam or clonazepam may be habit-forming and have been associated with a risk of dementia and should be avoided
- The “z-drugs” (e.g., Ambien) can cause parasomnias (sleepwalking and sleeptalking)
- All sleep-inducing medications can cause daytime somnolence or grogginess

**REM SLEEP BEHAVIOR DISORDER (RBD)**
- Dream sleep is known as rapid eye movement (REM) sleep because when we dream, the body is typically motionless other than eye movements
- In RBD, the body moves during REM sleep, resulting in dream enactment behavior

**Things to know**
- The dreams in RBD tend to be vivid and/or violent
- The patient often is protecting himself or a loved one against an aggressor
- The patient may thus kick, punch or otherwise injure their bedfellow
- Patients may jump out of bed and injure themselves

**Potential testing**
- Sleep study to differentiate between RBD and other parasomnias such as sleepwalking and sleeptalking
- Sleep study excludes sleep apnea as a cause or worsening of RBD

**Non-medication treatment**
- Reduce medications that can cause or exacerbate RBD
- Safety measures: avoid sharp objects by the bed
- Keep the bed low
- Padding around furniture near the bed
- Keep the door closed

**Medication options**
- Off label: Melatonin 3-12 mg
- Clonazepam 0.5-2 mg at bedtime

**Potential side effects**
- Daytime somnolence or grogginess
- Nighttime confusion if they awaken to use the restroom

**DEPRESSION**
- Not correlated with severity of motor symptoms
- Increased risk of suicidal thoughts

**Things to know**
- Tricyclic antidepressants (TCAs) can help for motor symptoms, drooling and sleep

**Potential testing**
- Sometimes bloodwork may help if fatigue is the main manifestation

**Non-medication treatment**
- Counseling
- Cognitive behavioral therapy
- Psychosocial support
- Physical activity

**Medication options**
- TCAs: Nortriptyline 75 mg / night
- SNRIs: Venlafaxine (Effexor) up to 225 mg / day
- Dopamine/NE reuptake inhibitor: Buproprion (Wellbutrin) up to 300 mg / day

**Potential side effects**
- TCAs can worsen confusion, orthostatic hypotension
- SSRIs can worsen PD symptoms
- Antidepressant side effects include sexual dysfunction, headache, fogginess, insomnia
### ANXIETY
- Not correlated with disease severity
- Can manifest as health anxiety, generalized worry, panic attacks, anxiety about meds wearing off
- Anxiety can worsen PD symptoms

<table>
<thead>
<tr>
<th>Potential testing</th>
<th>• Typically none</th>
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</table>
| Non-medication treatment | • Counseling  
• Cognitive behavioral therapy  
• Psychosocial support  
• Physical activity  
• Reduce medications that may worsen anxiety |
| Medication options | • Buspirone  
• Paroxetine (Paxil)  
• Citalopram (Celexa)  
• Mirtazapine (Remeron)  
• SNRIs: Venlafaxine (Effexor)  
• Off label: Gabapentin |
| Potential side effects | • Dizziness, drowsiness, tingling, nausea  
• Sexual dysfunction, increased sleep, increased appetite / weight gain (mirtazapine)  
• Imbalance, blurry vision |

### COGNITIVE DYSFUNCTION
- Can range in severity
- Changes in personality
- Delayed mental responses
- Impaired working memory
- PD-related dementia (PDD)

| Things to know | • In PDD, dementia comes on no earlier than a year after diagnosis of parkinsonism  
• In dementia with Lewy bodies (DLB), dementia comes on before or at the same time as parkinsonism  
• Differs from Alzheimer's disease in that memories can still be encoded, just harder to retrieve |
| Potential testing | • Neuropsychological evaluation (a battery of tests assessing memory, language, visuospatial function, and executive function)  
• Sleep study to exclude sleep apnea if there are risk factors such as snoring and obesity  
• Blood and urine tests if cognitive changes occur rapidly to exclude infection |
| Non-medication treatment | • Mental stimulation  
• Physical activity  
• Social support  
• Improved sleep  
• Discontinue medications that can cause confusion |
| Medication options | Rivastigmine (Exelon)  
• Oral: up to 4.5 mg twice a day  
• Patch: up to 9.6 mg/24 hours  
• Off label: Donepezil 10 mg at bedtime  
• Memantine 10 mg twice a day |
| Potential side effects | Rivastigmine/ donepezil:  
• Dizziness, diarrhea, weight loss, agitation, tremor  
• Application site redness from patch  
Memantine:  
• Dizziness, low blood pressure, confusion, headache, constipation, diarrhea |

### LOSS OF SENSE OF SMELL OR TASTE (ANOSMIA)

| Things to know | • Often precedes diagnosis of PD by many years |
| Potential testing | • UPSIT (smell testing)  
• CT of sinuses if there is history of injury or recurrent infection |
| Non-medication treatment | • Cook with stronger spices  
• Quit smoking  
• Ensure fire detectors and smoke alarms are properly working |
<p>| Medication options | • None indicated |</p>
<table>
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<tr>
<th>PSYCHOSIS</th>
<th>Things to know</th>
<th>Potential testing</th>
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<tr>
<td>• Illusions (misperception)</td>
<td>• Patients may not want to admit to these symptoms due to stigma</td>
<td>• Blood and urine tests if cognitive changes occur rapidly to exclude infection</td>
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<tr>
<td>• Hallucinations</td>
<td>• Can be very distressing to patient or caregiver</td>
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<td>• Typically visual, but can be auditory or tactile as well</td>
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<tr>
<td>• Delusions (fixed false belief)</td>
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<tr>
<td>• Paranoia</td>
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<thead>
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<th>Non-medication treatment</th>
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<tr>
<td>• Keep rooms well-lit during the day</td>
<td>Pimavanserin (Nuplazid) 34 mg daily, a novel serotonin inverse agonist which does not affect motor symptoms. Nuplazid may take up to 4 weeks to take effect</td>
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<td>• Good sleep habits</td>
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<tr>
<td>• Minimize clutter</td>
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<td>• Yearly vision exam</td>
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<thead>
<tr>
<th>Potential side effects</th>
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<tbody>
<tr>
<td>• Nausea</td>
<td>• Constipation</td>
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<tr>
<td>• Swelling</td>
<td>• Confusion</td>
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<tbody>
<tr>
<td>• Typically due to rigidity</td>
<td>• Can cause patients to limit physical activity</td>
<td>• Consultation with an orthopedic surgeon or sports medicine doctor</td>
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<tr>
<td>• Muscle aches due to tremor / dystonia</td>
<td>• Limited mobility can in turn exacerbate joint and muscle pain</td>
<td>• X-ray of affected joint</td>
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<tr>
<td>• Injury from falls</td>
<td>• Nerve pain: tingling, burning, shooting pain</td>
<td>• Blood and nerve test for neuropathy</td>
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<th>Non-medication treatment</th>
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<tr>
<td>• Physical therapy</td>
<td>Prescription / off label for nerve pain:</td>
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<tr>
<td>• Massage therapy</td>
<td>• Gabapentin</td>
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<td>• Pregabalin</td>
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<td>• Nortriptyline</td>
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<td>• NSAIDs: Gastric ulcers, kidney injury, bleeding, high blood pressure</td>
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<td>• Tylenol: Liver failure when taken at doses &gt; 3 grams / day</td>
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<tr>
<td>• Gabapentin/pregabalin: Sedation, dizziness, blurry vision</td>
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<tr>
<td>• Nortriptyline: Dry mouth, constipation, sedation, urinary retention</td>
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