

Medications

A Treatment Guide to Parkinson's Disease



About this book

This book is a practical guide about different types of prescription medications used to treat movement and non-movement symptoms caused by Parkinson's disease (PD). The information in this book will help you understand your medications and work with your doctor to adjust them as needed. **It is not meant to replace the advice of expert medical professionals involved in your care.**

Medications are a central part of managing PD but need to be combined with exercise and other types of therapies to maximize symptom relief and quality of life. Work with your healthcare team to find the right balance for you.

The Parkinson's Foundation is here to help. As you and your loved ones review this book, direct any questions to our Helpline specialists. Call [1-800-4PD-INFO \(1-800-473-4636\)](tel:1-800-4PD-INFO) or email Helpline@Parkinson.org.

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General Medication Information

Although there are general guidelines doctors use when prescribing medications, each person with Parkinson's disease (PD) must be individually evaluated to determine which drug or combination of medications is best for them. For some, a "first choice" drug might be a form of levodopa, and for others, an initial prescription may be given for a different medication.

It is common for people with to take a variety of medications at different doses and at different times of day to manage their unique symptoms. Taking the right medication on time, every time is critical to managing symptoms.

✓ TIPS

- Keep in mind that the choice of medication and dosages depend on a variety of factors, including symptoms (which vary from person to person), other health issues (and the medications used to treat them), as well as metabolism and age.
- Tell your healthcare team about any medication changes.
- Use a symptoms diary to note any side effects and report these to your doctor promptly.
- Do not abruptly stop or change your medications. Stopping medications suddenly can lead to serious complications and an increase in Parkinson's symptoms.
- Ask questions ... and take notes!

Generic vs. Brand-Name Drugs

A brand-name drug is a medication sold by a drug company under a specific name. Many medications are also available as generic drugs, which are often less expensive.

The U.S. Food and Drug Administration (FDA) requires a generic medication to have the same active ingredients as the brand name. For most people, generic versions work just as well as the brand names. However, if you notice a difference when switching from a brand name to generic, or if your brand-name medication is too costly, speak with your doctor.

Key Words

Getting familiar with these words can help you understand key concepts throughout the book.

Acetylcholine A brain chemical that plays an important role in movement and thinking (cognition). Acetylcholinesterase inhibitors increase acetylcholine levels, which may improve cognition. Anticholinergics, which block acetylcholine, can help reduce tremor but may cause confusion and cognitive issues, especially in older adults.

Brand-name medication A drug developed by a company with exclusive rights to sell and market the drug until the patent expires.

Clinical trial A research method that determines if treatments are safe and effective by testing how they work in people.

Cognitive Related to brain processes such as thinking, reasoning and memory.

Dopamine A type of chemical messenger (neurotransmitter) in the brain that is involved in movement, mood, motivation and more. People with Parkinson's have very low levels of dopamine in the brain.

Dopaminergic medication A type of medication that increase dopamine levels in the brain.

Dose A specified amount of medication taken at one time, such as one tablet of 25/100 mg carbidopa/levodopa.

Dosage A specified amount of medicine and how often to take it. For example, one tablet of 25/100 mg carbidopa/levodopa taken every three hours.

Food and Drug Administration (FDA) A U.S. federal agency that protects public health by overseeing the safety and effectiveness of products, including medications, medical devices and the nation's food supply.

Formulation Different variations of a medication, such as a capsule, tablet, gel or liquid. Formulations can change how a medication works, as with extended-release and immediate-release versions of the same drug.

Generic medication A medication with the same active ingredient as the brand name. Generic medications are usually less expensive.

Lewy bodies Deposits of a protein called alpha-synuclein in the brain that causes problems with movement, mood, thinking and behavior.

Mood chemicals Mood-regulating brain chemicals, including dopamine, norepinephrine and serotonin. Mood disorders, such as anxiety and depression, can occur when there is a chemical imbalance.

Neurodegenerative disorder A disease that involves a gradual loss of cells in the brain or spinal cord. Over time, this cell loss leads to increased symptoms and disability.

Neurotransmitter A chemical messenger that transmits signals from one nerve cell to another. Examples include dopamine, acetylcholine and norepinephrine.

Off-label Commonly refers to prescribing medication for a condition or symptom for which it has not received FDA approval. For example, donepezil (Aricept) — which is FDA-approved to treat Alzheimer's disease — is sometimes used to treat Parkinson's disease dementia.

"Off" time When symptoms worsen in between medication doses.

Over the counter Medications and devices available to purchase without a prescription, such as aspirin and Benadryl.

Side effect A secondary and usually negative or unwanted effect of a medication. Sometimes a medication can have beneficial side effects, such as antidepressants that cause sleepiness for someone with sleep problems.

1 About Parkinson's Disease

Let's review the basics:

- ▶ Parkinson's disease (PD) is a progressive neurodegenerative disorder that affects about 1 million people in the United States and 10 million people worldwide.
- ▶ PD symptoms are varied and usually develop slowly over time.
- ▶ Parkinson's is considered a movement disorder because it can cause tremor, slow movements (bradykinesia), stiffness (rigidity), muscle cramping (dystonia) and problems with balance and walking.
- ▶ Parkinson's can also cause many non-movement symptoms, such as depression, sleep issues, constipation and fatigue.
- ▶ Although there is no cure for Parkinson's at this time, many advances in treatment options continue to help people live better with PD.

How is PD diagnosed?

Parkinson's is a "clinical" diagnosis. This means that a person's history, symptoms and physical exam are used to make the diagnosis. There is no single lab or test that is commonly used to diagnose PD. However, brain imaging studies, such as an MRI or DaTscan, or an alpha-synuclein skin biopsy test can be used to support the diagnosis of Parkinson's or to rule out other medical conditions that can mimic PD.

How does the brain change in PD?

Dopamine is one of several chemical messengers brain cells use to send signals to each other. People with Parkinson's lose the ability to produce enough dopamine. After this was discovered in 1960, dopamine-replacement therapy using levodopa became — and remains — the gold-standard in managing Parkinson's movement symptoms.

The body's dopamine system is not the only one affected by Parkinson's. The disease process disrupts other brain networks, including those connected to mood, behavior and thinking (cognition).

Parkinson's is also linked to the abnormal clumping of a protein called alpha-synuclein in the brain. Researchers continue to study how PD affects brain networks and cells to improve our understanding of the disease and potential treatments.

Is PD inherited?

For most people, the cause of Parkinson's is unknown or "idiopathic." Researchers believe it is caused by a combination of genetic and environmental factors. Genetics can be linked to about 10-15% of Parkinson's.

There is no test that can accurately predict who will develop Parkinson's. Extensive genetic research is underway to continue to uncover the possible factors involved in disease development. Scientists are also seeking PD biomarkers (measurable features of disease progression).

Genetic testing can help people with Parkinson's understand and manage their condition and may contribute to research around new treatments and personalized or customized therapies. The Parkinson's Foundation offers genetic testing and genetic counseling at no cost for people with Parkinson's through its global study. Learn more at [Parkinson.org/PDGeneration](https://parkinson.org/PDGeneration).

2 Medications for Movement Symptoms

The three main (or cardinal) movement (or motor) symptoms in Parkinson's disease (PD) are slowness (bradykinesia), stiffness (rigidity) and tremor. Cramping (dystonia) and balance and coordination problems are also common movement symptoms. Although not everyone with PD will experience all of these symptoms, slowness plus either tremor or rigidity must be present to consider a diagnosis. Since movement symptoms are caused in large part by a lack of dopamine in the brain, medications used to treat these symptoms replace, mimic or boost the effect of dopamine. These medications may also improve some non-movement symptoms.

In this chapter, we will discuss the following medications:

- ▶ Levodopa
- ▶ Dopamine Agonists
- ▶ MAO-B Inhibitors
- ▶ COMT Inhibitors
- ▶ Adenosine A2A Antagonists
- ▶ Amantadine
- ▶ Anticholinergics

Levodopa

The most powerful PD medication is levodopa. Its development in the late 1960s represents one of the most important breakthroughs in Parkinson's treatment.

Quick Levodopa Facts

- Levodopa is generally viewed as the first-line drug for Parkinson's movement symptom management.
- Levodopa (in pill form) is absorbed into the blood from the small intestine and travels through the blood to the brain, where it is converted into dopamine.
- Dopamine itself cannot be used instead of levodopa to treat PD because its chemical structure does not cross the "blood-brain barrier," a biological screen that works to protect the brain from infection and harm.
- Levodopa is almost always given in combination with the drug carbidopa, which reduces or prevents the nausea that levodopa alone can cause.

Levodopa and the Gut

The gut slows down in PD. Delayed stomach (gastric) emptying — also known as gastroparesis — can delay the benefits of levodopa or make it less effective. Constipation (infrequent bowel movements) is another common issue in PD. For many people, drinking more water and eating fiber-rich foods, such as vegetables and whole grains, can help them stay regular. Gastroparesis can be more challenging to manage, but recommendations often include reducing fat and fiber and eating smaller meals. For both constipation and gastroparesis, it is important to consult with a dietician or nutritionist for dietary guidance. Read more about treatments and medications for gastrointestinal symptoms on pages 41-42.

Carbidopa/Levodopa Side Effects

Carbidopa/levodopa side effects vary significantly from person to person, but some of the most common are:

- Nausea and other gastrointestinal side effects
- Low blood pressure
- Dizziness
- Confusion
- Dyskinesia (see page 11)

Side effects are more common when beginning levodopa treatment or increasing the dose, but can happen at any point. Starting with a low dose and slowly increasing it as necessary to improve symptoms can help minimize side effects. This is especially helpful in older adults with Parkinson's, who may have a lower medication tolerance.

✓ TIP

Eating a cracker or a piece of toast with carbidopa/levodopa can reduce the frequency and intensity of nausea. For some people, adding extra carbidopa (Lodosyn) to each dose of carbidopa/levodopa can also help.

"Off" Time

As Parkinson's advances, people often experience symptom fluctuations throughout the day depending on how well their carbidopa/levodopa medication is working. "On" time happens when symptoms are under control. "Off" time refers to moments when symptoms are not well managed with medication. Read more about managing "off" time in Appendix A on page 54.

Dyskinesia

Uncontrolled, involuntary movements of the face, arms, legs or trunk, called dyskinesia, are a potential complication of using levodopa. The likelihood of developing dyskinesia is low in early Parkinson's and is usually mild if it does occur. On average, people taking carbidopa/levodopa develop dyskinesia around five years after starting levodopa. Some people will never experience this side effect. Severe dyskinesia that interferes with daily activities is less common. Risk factors for developing dyskinesia include younger age, lower body weight, being female or having more severe PD symptoms. Dopamine agonists and other PD medications that boost dopamine, discussed in the next sections, can also contribute to dyskinesia but to a lesser degree than levodopa.

✎ NOTE

Sometimes, the fear of dyskinesia can lead to not taking enough carbidopa/levodopa to control symptoms. Talk to your doctor if you have concerns.

If you are experiencing dyskinesia, you can work with your neurologist to find the right approach for you. Your neurologist may try to reduce your levodopa dose, remove other medications that enhance dopamine or add amantadine, a medication used to treat dyskinesia — or a combination of these approaches. Read more about amantadine on page 20.

In certain circumstances, if medication strategies are not successful, deep brain stimulation (DBS) or focused ultrasound might be considered to control dyskinesia.

Levodopa Medications

Levodopa is available in many forms, including immediate-release, controlled-release and extended-release. In addition to pills and capsules, it is also available as an intestinal gel and inhaled powder.

✎ NOTE

Substitution of a different form or strength of levodopa may lead to an under or overdose, so be careful renewing prescriptions at the pharmacy or when receiving medications in the hospital.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Carbidopa/levodopa immediate release (Sinemet)				
10/100, 25/100 or 25/250 mg tablets	150-2,000 mg of levodopa/day in separate doses	Nausea, low blood pressure, dizziness, confusion and dyskinesia	For PD symptoms (slowness, stiffness, tremor, etc.)	Typically starts working within 45 minutes
Carbidopa/levodopa immediate release (Dhivy)				
25/100 mg breakable tablets	Up to 8 tablets/day	Same as above	Same as above	Can be snapped in quarters or in half, which may be appropriate for people who split their pills
Carbidopa/levodopa controlled release (formerly Sinemet CR)				
25/100 or 50/200 mg tablets	200-2,400 mg of levodopa/day in separate doses	Same as above	Same as above	Designed to last longer but may not provide enough symptom relief for some people Often used before bed
Carbidopa/levodopa extended release (Rytary)*				
23.75/95, 36.25/145, 48.75/195 or 61.25/245 mg capsules	855-2,340 mg of levodopa/day in separate doses	Same as above	Same as above	May be appropriate for people with swallowing issues, as capsules can be opened and sprinkled over applesauce

*Extended-release carbidopa/levodopa capsules are not interchangeable with other carbidopa/levodopa products. For prescribing and dosing information to share with your doctor, visit [Parkinson.org/Medications](https://www.parkinson.org/Medications).

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Carbidopa/levodopa/entacapone (Stalevo) [see: entacapone in COMT inhibitors section]				
12.5/50/200, 18.75/75/200, 25/100/200, 31.25/125/200, 37.5/150/200 or 50/200/200 mg tablets	150-1,200 mg of levodopa/day in separate doses	Nausea, low blood pressure, dizziness, dyskinesia, behavioral changes, diarrhea and discolored urine	Replacement for immediate-release carbidopa/levodopa for people with end-of-dose wearing off	Combines carbidopa/levodopa and entacapone for convenience
Carbidopa/levodopa enteral suspension (Duopa) via surgically implanted tube in small intestine*				
4.86/20 per mL	Up to 2,000 mg of levodopa over 16 daytime hours	Nausea, low blood pressure, dizziness, dyskinesia and behavioral changes	For treatment of "on/off" fluctuations in people with advanced Parkinson's	May reduce dyskinesia
Levodopa inhalation powder (Inbrija)				
42 mg capsule	84 mg inhaled by mouth up to 5 times/day as needed	Same as above plus cough	Used with carbidopa/levodopa for "off" episodes	Does not go through the digestive tract, which may be helpful for people with slow stomach emptying or constipation

*For more information about carbidopa/levodopa enteral suspension and the pump, go to [Parkinson.org/Library](https://www.parkinson.org/Library) to read *Surgical Options: A Treatment Guide to Parkinson's Disease* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Carbidopa/Levodopa Questions and Answers

Q What symptoms does carbidopa/levodopa improve?

A For most people with Parkinson's, carbidopa/levodopa greatly improves movement symptoms — especially slowness and rigidity. The impact of levodopa on tremor is more difficult to predict: many people experience significant tremor improvement, but others may not.

Carbidopa/levodopa may also improve some non-movement symptoms, including pain, depression and anxiety. However, there are certain symptoms that may not respond well to carbidopa/levodopa, such as balance, swallowing and memory issues. Physical, speech, occupational and mental health therapists can be helpful for some symptoms that do not respond to medication.

Q How often does a person need to take carbidopa/levodopa?

A It is common early on in PD to take three doses of carbidopa levodopa immediate release (IR) evenly spaced throughout the day to manage symptoms. Symptoms typically start improving within 45 minutes and benefits can last for four hours or more. Some people are less sensitive than others to a medication dose that is late or skipped, but precise medication timing leads to the best symptom control.

As PD progresses, many people begin to take medication more frequently to reduce "off" time.

Q Does carbidopa/levodopa need to be taken with food?

A If you can tolerate carbidopa/levodopa on an empty stomach, the ideal time to take this medication is 30-60 minutes before a meal.

This gives the medication a head start into the gut and then the blood stream, so it's not competing with food. Protein-rich foods (meat, fish, eggs, dairy, beans, nuts), in particular, are more likely to interfere with levodopa. Food-levodopa interactions are usually not as noticeable for people who have early Parkinson's.

NOTE

Getting enough protein in your diet is necessary for building muscle and maintaining overall good health. If you find that taking your carbidopa/levodopa medication close to mealtimes reduces its effectiveness, work with your doctor to make schedule adjustments — but do not eliminate protein from your diet.

Q Is it better to delay taking carbidopa/levodopa as long as possible?

A Research shows that while levodopa does not slow PD, starting the medication early is safe and can significantly improve quality of life by decreasing PD symptoms.

Q Does carbidopa/levodopa stop working over time?

A Carbidopa/levodopa does not stop working. However, after taking it for some time — typically years — you may notice more "off time" before your next dose. This is usually caused by the gradual progression of the disease. An adjustment to medications or medication schedule is often helpful. Talk with your doctor if you notice your medication wearing off early.

Dopamine Agonists

Unlike levodopa, which converts into dopamine in the brain, dopamine agonists mimic the effect of dopamine. They can be used in early treatment of PD on their own, or later in combination with carbidopa/levodopa. Compared to levodopa, dopamine agonists generally provide less benefit for movement symptoms, but they are longer acting, which may help reduce “off” time and improve levodopa benefits.

Dopamine Agonist Side Effects

Many of the side effects of dopamine agonists are similar to those of carbidopa/levodopa, but dopamine agonist use is less likely to cause or contribute to dyskinesia. In addition, certain side effects, such as excessive daytime sleepiness, hallucinations (seeing something that is not there), confusion and leg swelling, occur more commonly with dopamine agonists than with levodopa. Older adults with PD are particularly sensitive to experiencing confusion and hallucinations with dopamine agonist therapy.

Impulse control disorders (ICDs), which involve behaviors such as uncontrolled gambling, increased sexual urges (hypersexuality) and excessive eating and shopping, commonly occur as a result of dopamine agonist therapy. These disorders may also lead to a type of compulsive, repetitive activities, called punding. Punding can include an excessive need to organize, sort or collect items. Levodopa therapy can also lead to impulse control disorders, but less commonly than dopamine agonists.

The exact reason why dopamine agonist therapy can lead to ICDs isn’t fully understood. It is most likely related to overstimulating dopamine receptors in the part of the brain responsible for controlling impulses.

The person experiencing the impulse control issue may not be able to see these behaviors in themselves, so the healthcare team and care partners need to be on the lookout for these behaviors.

Dopamine Agonist Medications

Dopamine agonists are available in immediate and long-acting versions. There is also a patch form, as well as a quick-acting, injectable rescue medication.

NOTE

Taking the proper dose of dopamine agonist medication is important. Missing just one dose may lead to withdrawal symptoms, such as anxiety, drug cravings, excessive sweating, fatigue, orthostatic hypotension (low blood pressure) or pain.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Ropinirole [formerly Requip]				
0.25, 0.5, 1, 2, 3, 4 or 5 mg tablets	9-24 mg total/day in 3 separate doses	Dizziness, leg swelling, nausea, sleep attacks, confusion and behavioral changes, including compulsive behaviors	For PD symptoms (slowness, stiffness, tremor, etc.) and restless legs syndrome (RLS)	Has milder effect than carbidopa/levodopa but can be longer lasting
Longer-acting form available				Often used in early PD or combined with carbidopa/levodopa
Pramipexole (Mirapex)				
0.125, 0.25, 0.5, 0.75, 1 or 1.5 mg tablets	1.5-4.5 mg total/day in 3 separate doses	Same as above	Same as above	Same as above
Longer-acting form available				
Rotigotine (Neupro)				
2, 4, 6 or 8 mg patches	4-8 mg once/day	Same as above, plus skin irritation	Same as above	Same as above plus does not pass through the digestive tract, which may be helpful for people with slow stomach emptying, swallowing issues or constipation
Apomorphine subcutaneous injection (Apokyn)				
0.1-0.6 mL	Used as needed, up to 5 times per day	Same as other dopamine agonists, plus redness or bruising at the injection site	“Rescue” or on-demand medication for wearing-off episodes	Can start working within 10 minutes and last up to 90 minutes

MAO-B Inhibitors

Monoamine oxidase-B (MAO-B) is an enzyme that breaks down dopamine. An MAO-B inhibitor blocks that chemical breakdown, increasing available dopamine. MAO-B inhibitors can modestly improve PD movement symptoms.

MAO-B inhibitors are useful on their own for PD movement symptoms, or as an add-on to other medications, including levodopa. When used with other medications, MAO-B inhibitors may reduce "off" time.

MAO-B Side Effects

The most common side effects of MAO-B inhibitors include mild nausea, dry mouth, lightheadedness and constipation.

When MAO-B inhibitors are prescribed, pharmacists often warn people about interactions with other drugs, especially antidepressants. In reality these type of reactions between an MAO-B inhibitor and other drugs are rare. If you are taking an MAO-B inhibitor, review potential new medications for possible interactions with your doctor.

These medications and supplements should always be avoided by people taking MAO-B inhibitors:

- Meperidine (Demerol)
- Tramadol (Ultram)
- Methadone (Methadose)
- Cyclobenzaprine (Amrix, Fexmid, Flexeril)
- St. John's Wort
- Dextromethorphan

MAO-B Medications

Tablet, capsule and an orally disintegrating tablet formulation that dissolves on the tongue are available.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Selegiline (L-deprenyl, Eldepryl)				
5 mg capsules or tablets	5 mg twice/day at breakfast and lunch	Mild nausea, dry mouth, dizziness and constipation	For increasing benefits of carbidopa/levodopa	Can have stimulating effects, which can benefit some people but cause jitteriness, confusion or sleep issues for others
Also available as an orally disintegrating tablet				
Rasagiline (Azilect)				
0.5 or 1 mg tablets	Up to 1 mg once daily	Same as above	Same as above	Does not have stimulating effects
Safinamide (Xadago)				
50 or 100 mg tablets	Up to 100 mg once daily	Same as above	For increasing benefits of carbidopa/levodopa and decreasing "off" time	Same as above

COMT Inhibitors

Catechol-O-methyltransferase (COMT) is an enzyme that deactivates levodopa in the bloodstream before it gets to the brain. COMT inhibitors block this enzyme, so more levodopa is available to get into the brain. This can increase levodopa benefits and reduce "off" time.

NOTE

COMT inhibitors are always taken with carbidopa/levodopa.

COMT Inhibitor Side Effects

COMT inhibitors generally have minimal side effects, though they may intensify some levodopa-related side effects, particularly dyskinesia.

COMT Inhibitor Medications

In addition to the three COMT inhibitors below, carbidopa/levodopa/entacapone (listed in the carbidopa/levodopa medication table) combines three medications in one pill.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Entacapone (Comtan)				
200 mg tablets	200 mg tablet with each dose of levodopa/carbidopa	Increased side effects of carbidopa/levodopa* plus diarrhea	For increasing benefits of carbidopa/levodopa and decreasing "off" time	May turn urine and other bodily fluids a reddish-brown color
Opicapone (Ongentys)				
25 or 50 mg capsules	50 mg once/day at bedtime	Increased side effects of carbidopa/levodopa*	Same as above	Should avoid eating food one hour before and one hour after taking
Tolcapone (Tasmar)				
100 mg tablets	100 mg tablet 3 times/day	Increased side effects of carbidopa/levodopa* plus diarrhea and liver damage	Same as above	Rarely used due to potential for serious side effects

*For more information about carbidopa/levodopa side effects, see page 10.

Amantadine

Amantadine is used to treat PD movement symptoms and is sometimes prescribed on its own in early stages of PD when symptoms are mild. It is more commonly used to reduce dyskinesia. Its path through the brain is not fully known, but it likely impacts multiple neurotransmitters (chemical messengers) — including dopamine and glutamate — to achieve its benefits.

Amantadine Side Effects

The most frequent side effects of amantadine are nausea, dry mouth, lightheadedness, insomnia, confusion, swollen feet and hallucinations.

Amantadine Medications

There are immediate-release and extended/delayed formulations that contain amantadine as the active ingredient. Amantadine is cleared from the body by the kidneys, so people with kidney problems may require a lower dose.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Amantadine				
100 mg capsules Also available in liquid form	200 mg capsules daily	Nausea, insomnia, lightheadedness, confusion, swollen feet, dry mouth, hallucinations	For levodopa-induced dyskinesia and PD symptoms	May cause a net-like purplish discoloration of the skin on the legs
Extended-release amantadine (Osmolex ER)				
129, 193 or 258 mg tablets	129-322 mg once/day upon waking	Same as above	Same as above	ER medications should not be split, crushed or chewed because this can release the medication all at once
Extended-release amantadine (Gocovri)				
68.5 or 137 mg capsules	137-274 mg once/day at bedtime	Same as above	Same as above and used for the treatment of "off" time	Same as above

Anticholinergics

The neurotransmitters acetylcholine and dopamine maintain a delicate balance in the healthy brain. As Parkinson's advances, the loss of dopamine-producing cells disrupts this balance. Anticholinergics potentially restoring some balance. This can result in mild relief for movement symptoms, particularly tremor.

Anticholinergic Side Effects

Anticholinergic medications must be used with caution. They can cause significant side effects, particularly in older adults, and should not be used by this age group. Research from the Parkinson's Foundation shows an association between anticholinergic use and worsening cognition (thinking and memory).

Anticholinergic Medications

Tablet, capsule and liquid forms are available, depending on the medication.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Trihexyphenidyl [formerly Artane]				
2 or 5 mg tablets Also available in liquid form	1-2 mg 2-3 times/day	Confusion, drowsiness, memory issues, hallucinations, dry mouth, increased heart rate, urinary retention and dizziness	For tremor and dystonia, especially in Young Onset PD	Should be avoided in older adults
Benzotropine (Cogentin)				
0.5 mg capsule 1 or 2 mg tablets	Up to 6 mg tablets taken at bedtime or divided into 2-3 doses per day	Same as above	Same as above	Same as above

Adenosine A2A Antagonist

Istradefylline (Nourianz) is an adenosine A2A receptor antagonist used in combination with carbidopa/levodopa to manage "off" time in Parkinson's.

Although istradefylline does not boost or increase dopamine, it can contribute to dyskinesia in some people.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Istradefylline (Nourianz)				
20 or 40 mg tablets	20-40 mg tablets once/day	Dyskinesia, insomnia, hallucinations and dizziness	Combined with carbidopa/levodopa to manage "off" time	Should be taken soon after waking in the morning to avoid nighttime sleep disruptions

3 Medications for Non-Movement Symptoms

In addition to movement (or motor) symptoms such as slow movements (bradykinesia), tremor, stiffness (rigidity) and balance issues, most people with Parkinson's disease (PD) develop other symptoms related to PD. These symptoms are diverse and collectively known as non-movement (or non-motor) symptoms. Non-movement symptoms are common in Parkinson's. In recent studies, nearly 100% of people with PD reported experiencing at least one or more non-movement symptoms. Studies also show that healthcare professionals often miss the signs. The following PD non-movement symptoms and their treatments are discussed in this chapter:

- ▶ Mood Disorders: Depression and Anxiety
- ▶ Cognitive Impairment and Dementia
- ▶ Psychosis (Hallucinations and Delusions)
- ▶ Sleep Disorders
- ▶ Postural Low Blood Pressure (Orthostatic Hypotension)
- ▶ Gastrointestinal Symptoms: Nausea and Vomiting, Constipation, Bloating or Feeling Full
- ▶ Urinary Symptoms
- ▶ Drooling
- ▶ Sexual Dysfunction
- ▶ Seborrheic Dermatitis (a skin condition)
- ▶ Excessive Sweating
- ▶ Pain

NOTE

The tables throughout chapter 3 list examples of the most common medications used to treat non-movement symptoms. They are not all-inclusive lists.

Mood Disorders

Research estimates that at least 50% of people with PD will experience some form of depression during their Parkinson's journey and up to 40% will experience an anxiety disorder. Parkinson's Foundation research found that taken together, mood, depression and anxiety have the greatest impact on well-being — even more than common movement symptoms.

There are medication and non-medication approaches available to treat PD-related mood symptoms and disorders. Often, the most successful approaches include a combination of therapies, such as medication, counseling or psychotherapy (talk therapy) and lifestyle changes.

Depression & PD

Depression is an often under-recognized PD symptom. Depression can occur before movement symptoms, at the time of diagnosis or as Parkinson's progresses. Though not completely understood, the cause is likely related to an imbalance of mood chemicals in the brain, including dopamine, serotonin and norepinephrine.

Along with "feeling blue," depression symptoms can include:

- Insomnia or excessive sleeping
- Reduced energy
- Loss of interest or pleasure in normal activities
- Reduced ability to concentrate
- Difficulty engaging with others
- Sexual dysfunction
- Loss or gain of appetite and weight
- Feelings of guilt and self-pity
- Thoughts of death or suicide

Anxiety & PD

Similar to depression, anxiety can appear at any stage of Parkinson's. Some people experience depression and anxiety. Symptoms of anxiety may include:

- Feelings of unease
- Jitteriness
- Worry or panic
- Difficulty breathing or swallowing
- Heart fluttering
- Shaking
- Cold sweats

Anxiety can be related to movement symptoms. For example, tremor or freezing due to an "off" episode while in a social situation might cause anxiety or embarrassment; this anxiety can worsen symptoms, creating a vicious cycle. Managing "off" time may help reduce anxiety.

There are several types of anxiety disorders:

- **Generalized anxiety:** Excessive worry throughout most of the day without dramatic fluctuation
- **Obsessive-compulsive disorder (OCD):** Repetitive thoughts or ideas that cause anxiety followed by behaviors that relieve those feelings
- **Social avoidance:** Desire to avoid social situations and interactions due to anxiety or embarrassment.
- **Panic attacks:** Brief periods of intense anxiety which often causes physical symptoms of fear, sweating, dizziness, racing heart, chest pain or discomfort and tremor.

NOTE

Some PD medications, like dopamine agonists, can worsen obsessive-compulsive behaviors.

Non-Medication Treatments for Depression and Anxiety

For many people with PD, psychotherapy or counseling are key components of treating depression and anxiety. Parkinson's Foundation research found that medication plus talk therapy was 25% more effective at resolving symptoms than medication alone among people with PD who experienced depression for at least two years.

Cognitive behavioral therapy (CBT) is an effective type of psychotherapy that can be done one-on-one or in a group. It focuses on changing thought patterns and behavior related to depression and anxiety. This type of therapy can be particularly helpful in managing mood and changes related to PD.

Exercise and mindfulness techniques, such as yoga and meditation, can also improve depression and anxiety.

Electroconvulsive therapy can be considered for people with severe depression who do not respond to drugs. It is generally safe and effective when managed by experts and may also temporarily improve movement symptoms.

Your healthcare team can help you find the right treatment, therapies and support. They might refer you to a psychologist, social worker or other mental health professional.

NOTE

Many people experience stronger symptoms of depression or anxiety as PD medications wear off near the end of a dose. During an "off" period, people commonly experience irritability, anxiety or a general state of unease or dissatisfaction with life. If you or someone close to you notices a pattern of mood changes associated with "off" periods and the timing of your PD medication, talk to your neurologist about the possibility of adjusting or rescheduling your medications.

Medications for Depression and Anxiety

The same medications are used to treat depression in people with and without PD. Among the most common classes of antidepressant medications are selective serotonin reuptake inhibitors (SSRIs). Serotonin-norepinephrine reuptake inhibitors (SNRIs) and atypical antidepressants are also used to treat depression.

Doctors occasionally use older tricyclic antidepressants, such as amitriptyline (Elavil) and nortriptyline (Pamelor), in people with PD with sleep problems. Typically these medications are prescribed for younger people, because in older adults they may cause confusion and other side effects.

Most of the medications used to treat depression, including SSRIs, SNRIs and atypical antidepressants, may also improve anxiety. There are also anti-anxiety medications for general anxiety disorder, situational anxiety and for addressing symptoms of panic and worry.

✓ TIP

Some antidepressant side effects can be helpful for other PD symptoms. For example, if you experience insomnia, your doctor might recommend nighttime dosing of a medication that causes sleepiness or suggest a medication that causes dry mouth to reduce drooling.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Selective Serotonin Reuptake Inhibitors (SSRIs)				
Escitalopram (Lexapro)				
5, 10, or 20 mg tablets	10-20 mg once/day	Headache, nausea, diarrhea, drowsiness, insomnia, dry mouth, sweating, jitteriness, decreased sex drive, weight gain or loss	Depression and anxiety	The side effects of weight loss or weight gain may be beneficial to some people
Sertaline (Zoloft)				
25, 50 or 100 mg tablets Liquid form also available	25-200 mg once/day	Same as above	Same as above	Same as above

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)				
Duloxetine (Cymbalta)				
20, 30, 40 or 60 mg capsules	30-60 mg once/day	Nausea, dry mouth, dizziness, headache, excessive sweating, constipation, trouble sleeping, decreased sex drive	Depression and anxiety	The side effect of dry mouth may benefit some people experiencing drooling
Venlafaxine (Effexor)				
25, 37.5, 50, 75 or 100 mg tablets Longer-acting form also available	25-75 mg twice/day	Same as above plus may raise blood pressure	Same as above	Same as above
Atypical Antidepressants				
Bupropion (Wellbutrin)				
75 or 100 mg tablets Longer-acting forms also available	75-150 mg 3 times/day	Dry mouth, trouble sleeping, headache, nausea, constipation, confusion, dizziness and weight loss	Depression and anxiety	Notable for lack of sexual side effects
Mirtazapine (Remeron)				
15, 30 or 45 mg tablets Orally disintegrating tablets also available	15-45 mg once/day at bedtime	Drowsiness, dizziness, increased appetite, weight gain, constipation and vivid dreams	Same as above	Same as above

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
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Benzodiazepines

Alprazolam (Xanax)

0.25, 0.5, 1, 2 or 3 mg tablets or 1 mg/mL oral solution	0.25-1 mg 3-4 times/day	Drowsiness, tiredness, lightheadedness, depression, headache, confusion, dizziness and blurred vision	Anxiety	People may build up a tolerance and need a higher dose for the same effect
Longer-acting form also available				

Clonazepam (Klonopin)

0.5, 1 or 2 mg tablets	0.25-2 mg up to 3 times/day	Same as above	Same as above	Same as above
Orally disintegrating tablets also available				

Lorazepam (Ativan)

0.5, 1 or 2 mg tablets	0.5-2 mg up to 3 times/day	Same as above	Same as above	Same as above
Liquid form also available				

Other Anti-Anxiety Medication

Buspirone (Buspar)

5, 7.5, 10, 15 or 30 mg tablets	5-15 mg twice/day	Dizziness, drowsiness, dry mouth, nausea and headache	Generalized anxiety disorder	May not lead to dependence or require higher doses for the same effect
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Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
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Propranolol (Inderal)

10, 20, 40, 60 or 80 mg tablets	10-40 mg up to 3 times/day as needed	Decreased heart rate, depression and worsening of preexisting asthma	Taken as needed for situational anxiety	Typically prescribed to lower blood pressure but is also used to treat anxiety
Liquid form also available				

NOTE

It can take several weeks to experience the full benefits of antidepressant and anti-anxiety medications. Finding the right medication and dose often involves some trial and error.

For more information about mood and PD, visit Parkinson.org/Library to read or listen to *Mood: A Mind Guide to Parkinson's* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**. Non-medication approaches for apathy (ongoing lack of interest or motivation) are discussed in this book.

Cognitive Impairment and Dementia

Cognitive impairment is when a person has trouble remembering, learning new things, concentrating or making decisions that affect everyday life. People with PD are up to six times more likely to experience some degree of cognitive impairment compared to others their age.

Thinking changes in Parkinson's range from mild to more severe. PD-related thinking changes may affect:

- Mental processing speed
- Attention or concentration, such as losing one's train of thought in conversation
- Problem solving, decision-making, multitasking and planning
- Short-term memory
- Language production, including difficulty finding the right words

Mild Cognitive Impairment

Between 25 to 50% of people with PD experience mild cognitive changes that affect attention, problem solving, visual and spatial perception and memory. These changes are greater than those caused by normal aging but do not significantly impact daily living for everyone with PD.

Parkinson's Disease Dementia

As Parkinson's progresses, people with PD can develop more significant or severe memory and thinking problems. When these problems interfere with daily life and independence, they are diagnosed as dementia. Parkinson's disease dementia (PDD) refers to dementia caused by PD.

NOTE

Mood, sleep, medications and medical problems sometimes cause symptoms that can seem like dementia.

Dementia With Lewy Bodies

A closely related parkinsonism disorder — dementia with Lewy bodies (DLB) — is similar to PDD but differs in several important ways. The main difference in making the diagnosis of DLB versus PDD is timing. PDD is diagnosed when serious cognitive symptoms develop years after movement symptoms. In DLB, significant cognitive symptoms or mental fluctuations appear early on, often alongside movement symptoms. Other defining features of DLB include shifting awareness (periods of mental clarity alternating with periods of confusion, distractibility and sleepiness), varying levels of attention span, visual hallucinations and problems with spatial orientation — the awareness and ability to adapt to one's surroundings.

Diagnosis of Cognitive Changes

If you or your loved one with PD experiences cognitive changes, your doctor or healthcare team should complete a thorough medical workup. This can identify temporary and treatable causes.

If there is a sudden cognitive change, the doctor will consider other causes, such as an infection (usually of the lungs or bladder), vitamin deficiency, dehydration, thyroid disease, drug intoxication, constipation, sleep deprivation, strokes or head injury from a fall.

NOTE

A careful evaluation of current medications is always important in evaluating cognitive changes. Some PD medications and other drugs, for example opioid pain medications, can cause symptoms of confusion, especially in older adults. Pay particular attention to anticholinergics, amantadine and dopamine agonists.

Medications for Dementia

There are three different classes of medications typically used to treat PD-related dementia: Acetylcholinesterase inhibitors, glutamate antagonists and stimulants. Medications for dementia do not reverse cognitive decline but may improve quality of life and dementia symptoms.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Acetylcholinesterase Inhibitors				
Donepezil (Aricept)				
5, 10 or 23 mg tablets Orally disintegrating tablets also available	5-23 mg once/day at bedtime	Nausea, diarrhea, headache, muscle cramps, vomiting, insomnia, slow heart rate, and dizziness	Dementia	May be helpful for psychosis
Galantamine (Razadyne)				
4, 8 or 12 mg tablets Long-acting and liquid forms also available	8-12 mg twice/day	Same as above	Same as above	Same as above
Rivastigmine (Exelon)				
1.5, 3, 4.5 or 6 mg capsules Patch also available	1.5-6 mg twice/day	Same as above	Same as above	Same as above
Glutamate Antagonists				
Memantine (Namenda)				
5 or 10 mg tablets Long-acting and liquid forms also available	5-20 mg once/day (If more than 5 mg/day, give twice/day)	Dizziness, headache, confusion and constipation	Dementia	May be helpful for psychosis, plus often used in combination with acetylcholinesterase inhibitors

For more information about thinking changes and PD, visit Parkinson.org/Library to read or listen to *Cognition: A Mind Guide to Parkinson's* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Psychosis

Between 20-40% of people with PD report having hallucinations or delusions. PD-related psychosis usually starts with mild symptoms, but people with PD can also experience severe confusion (delirium), hallucinations and delusions at some point during the course of their disease.

- **Hallucination:** when a person believes they see, hear, smell or feel something that is not actually there.
- **Illusion:** a misperception of reality that involves misidentifying something that is there. For example, a belt may appear to be a snake.
- **Delusion:** a form of self-deception in which a person develops a false belief despite strong evidence that the belief is untrue. For example, a person may believe someone is stealing from them even though nothing has been taken or is missing.
- Feeling a "sense of presence" is also fairly common. For example, a person may feel like someone else is in the room with them when no one else is there.

Evaluating Hallucinations & Delusions

If you are experiencing delusions or hallucinations, you and your healthcare team should work together to take the following steps:

- 1 Fully understand the behavior.** How frequent and severe are your hallucinations? Do they occur during the day and night? Do you recognize that your hallucinations are not real? Does the problem pose a physical, emotional or financial threat to you or your family? Have your memory, personality or concentration been changing?
- 2 Identify other medical problems you are experiencing.** Other medical problems could trigger a decline in cognitive ability. For example, are there any signs of infection such as fever, cough, painful urination or diarrhea? Are there symptoms of underlying depression? Are there other medical conditions that require attention, such as dehydration or disorders of the heart, liver or kidneys?
- 3 Review all PD medications you are taking, paying special attention to any recent medication changes.** PD medications have the potential to cause mental clouding and psychosis (hallucinations and delusions), especially at high doses or in combination with other risk factors, such as older age and underlying cognitive impairment. Your healthcare team can evaluate whether your symptoms may be medication related.
- 4 Discuss any other medications or supplements you are taking.** Have any new medications been started — sleep aids, opioid pain medications, antibiotics, steroids, antidepressants or anxiety medications? Have doses of existing medications changed recently? Could drugs, marijuana or alcohol be a factor? Consider over-the-counter medications, too. Based on your answers, your healthcare team can suggest the best course of treatment.

Generally, doctors start by decreasing or stopping PD medications that provide little benefit compared to their side effects. Anticholinergics, amantadine, dopamine agonists, MAO-B and COMT inhibitors are usually reduced in this order. Levodopa, considered the most effective medication for treating PD movement symptoms, is usually the last medication to be reduced.

Antipsychotic Medications for Hallucinations & Delusions

Older antipsychotic medications work primarily by blocking dopamine, which can worsen PD movement symptoms. Newer antipsychotic medications — pimavanserin (Nuplazid), quetiapine (Seroquel) and clozapine (Clozaril) — are less likely to worsen PD symptoms.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Clozapine (Clozaril)				
25 or 100 mg tablets	Starting with 12.5 mg and up to 50 mg once or twice/day	Drowsiness, drooling, tachycardia (fast heart rate), dizziness, constipation, low blood pressure and headache	Psychosis (hallucinations and delusions)	Blood tests for white blood cell counts required
Pimavanserin (Nuplazid)				
34 mg capsule 10, 17 mg tablets	34 mg once daily	Confusion, swelling of hands or feet, sudden dizziness, shortness of breath, fast heart rate	Same as above	Unlike other antipsychotic medications, does not affect movement symptoms
Quetiapine (Seroquel)				
25, 50, 100, 200, 300 or 400 mg tablets Long-acting and form also available	12.5-100 mg once or twice/day	Dizziness, drowsiness, dry mouth, low blood pressure, confusion, stomach pain and weight gain	Same as above	Higher doses may worsen PD symptoms

For more information about psychosis and PD, visit Parkinson.org/Library to read or listen to *Psychosis: A Mind Guide to Parkinson's* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Sleep Disorders

Sleep disorders that commonly affect people with PD include:

- Restless legs syndrome (RLS)
- Periodic limb movements of sleep (PLMS)
- REM sleep behavior disorder (RBD)
- Insomnia
- Excessive daytime sleepiness (EDS)

Sleep diagnostic tools can help identify daytime sleepiness and provide clues to sleep disruptions during the night. For example, the Epworth Sleepiness Scale is a questionnaire that can be completed at home that examines your tendencies to fall asleep during daytime activities, such as driving or watching television.

An overnight sleep evaluation by a trained specialist (often a sleep doctor) can provide more information and may be recommended if your healthcare team suspects you have sleep apnea, a breathing disorder that can affect or even stop breathing during the night. Typically, the evaluation will monitor your heart rate, breathing activity, snoring, involuntary movements and sleep quality.

Restless Legs Syndrome & Periodic Limb Movements of Sleep

Restless legs syndrome (RLS) is a common disorder characterized by unpleasant sensations in the legs — often described as burning, creeping, tingling, tugging or “like insects crawling inside the legs.” RLS symptoms occur most commonly in the evening or at night when seated or lying down. Some people with PD confuse RLS with levodopa-related dyskinesia; however, restless legs syndrome is an abnormal sensory perception, while dyskinesia involves actual movement of the limbs that comes and goes depending on levodopa levels.

Periodic limb movements of sleep (PLMS) are episodes of repetitive, jerky, involuntary leg movements during sleep. Like many sleep disorders, the bed partner is likely to be more aware of the involuntary movements than the person with the symptom. RLS and PLMS often occur together in people with PD.

Your doctor may refer you for an overnight sleep study if the cause of the sleep disturbances is not clear.

Medications for RLS and PLMS

Extra nighttime doses of long-acting PD medications, such as Sinemet CR or a dopamine agonist, may bring relief. Other prescription drug treatment options include gabapentin enacarbil (Horizant), pregabalin (Lyrica), benzodiazepines — such as clonazepam (Klonopin) — and low-dose opioid pain medications. In addition, your doctor may order bloodwork to check levels of ferritin (a blood protein containing iron), which can indicate the need for iron replacement.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Gabapentin enacarbil (Horizant)				
300 and 600 mg extended-release tablets	600 mg once/day, taken at around 5 pm	Sleepiness, dizziness, nausea	Restless legs syndrome and periodic limb movements of sleep	Can take several weeks to reach full effect
Pregabalin (Lyrica)				
25, 50, 75, 100, 150, 200, 225 and 300 mg capsules Liquid form also available	Up to 600 mg 2-3 times per day	Dizziness, drowsiness, dry mouth, swelling, blurred vision, weight gain and difficulty with thinking and concentration	Same as above	May require blood testing

REM Sleep Behavior Disorder

During the rapid eye movement (REM) sleep phase — when dreaming normally occurs — people with REM sleep behavior disorder (RBD) act out dreams. RBD involves active behaviors, such as kicking, fighting, yelling or thrashing. The person experiencing RBD may even walk around or fall out of bed during REM sleep. In addition to reports shared by the person with Parkinson's or a bed partner, an overnight sleep study can confirm an REM sleep behavior disorder diagnosis. RBD is often present for months or years before the onset of PD movement symptoms.

Medications for REM Sleep Behavior Disorder

For treatment of RBD, low-dose benzodiazepines or melatonin at bedtime may help.

Insomnia

Insomnia is an inability to fall asleep or stay asleep. In addition to normal nighttime awakening, people with PD may experience depression, anxiety and a change in their sleep-wake cycle, all of which can affect sleep. Tremor, stiffness and difficulty moving in bed may cause significant sleep disruptions, which can lead to sleep deprivation (getting less than the needed seven to nine hours of nightly sleep) and daytime sleepiness. Napping during the day can then affect the normal sleep cycle and result in difficulty sleeping at night.

Non-Medication Treatments for Insomnia

Treating insomnia can be challenging and usually requires a many-sided approach. It is important that you create a regular sleep-wake schedule and build healthy sleep habits, including:

- Establishing regular bed and wake-up times
- Reducing caffeine and alcohol intake
- Participating in cognitive behavioral therapy (CBT) provided by a psychologist or trained healthcare professional
- Limiting daytime naps
- Avoiding food and drink within several hours of bedtime
- Limiting time in bed for activities outside of sleep or sexual activities, such as reading, doing work or watching television

Medications for Insomnia

You may be advised to adjust your medications. If "wearing-off" symptoms such as stiffness and tremor interrupt your sleep, your doctor might recommend an extra dose of carbidopa/levodopa late in the evening or if you wake up during the night. Some people with PD use controlled-release carbidopa/levodopa (Sinemet CR) or extended-release carbidopa/levodopa (Rytary) at bedtime for this reason.

If necessary, your healthcare team might add medications to help you fall asleep or stay asleep at night (or stay awake during the day). Some antidepressant drugs with sedative properties can promote sleep at low doses (see pages 26-29 for antidepressant information).

Other prescription medications, such as zolpidem (Ambien), can promote sleep but are associated with significant safety risks, and are not typically prescribed for people with PD.

✓ TIP

Use any sleep aid cautiously, especially if you are an older adult, as getting up in the middle of the night while groggy may lead to falls.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Clonazepam (Klonopin)				
0.5, 1 or 2 mg tablets Orally disintegrating tablets also available	3-10 mg once/day at bedtime	Drowsiness, tiredness, lightheadedness, depression, headache, confusion, dizziness and blurry vision	REM Sleep Behavior Disorder (RBD)	Can cause withdrawal symptoms when stopped suddenly

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Melatonin				
1, 3, 5 or 10 mg tablets	3-10 mg once/day at bedtime	Drowsiness and nausea	Insomnia, RBD	Available over the counter
Mirtazapine (Remeron)				
7.5, 15, 30 or 45 mg tablets	7.5-15 mg once/day at bedtime	Drowsiness, increased appetite, vivid dreams, headache	Insomnia	Both a sleep aid and an antidepressant
Trazodone (Desyrel)				
50, 100, 150 or 300 mg tablets	50-100 mg once/day at bedtime	Nausea, dry mouth, dizziness, drowsiness, fatigue, blurry vision, headache	Insomnia	Same as above

Excessive Daytime Sleepiness

Excessive daytime sleepiness (EDS) may be a symptom of Parkinson's or a result of insomnia during the night, sleep apnea or PD medications. When EDS is caused by insomnia, creating a regular sleep-wake schedule and improving sleep habits can help. Refer to the Non-Medication Treatment for Insomnia section on page 36 for more information.

People with significant cognitive difficulties are more likely to experience EDS. Daytime "sleep attacks" are also common and involve feeling a sudden and irresistible urge to sleep, or actually falling asleep without feeling sleepy beforehand. Sleepiness and sleep attacks during the day occur more frequently with dopamine agonists.

Medications for EDS

Although not specifically indicated for excessive daytime sleepiness in people with PD, certain stimulants can be tried at low doses under the close supervision of a doctor to increase daytime wakefulness and alertness.

In addition, selegiline, an MAO-B inhibitor with stimulating side effects, is sometimes used to counteract excessive daytime sleepiness.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Methylphenidate (Ritalin)				
5, 10 or 20 mg tablets	5-15 mg 2 or 3 times/day	Rapid or irregular heart rate, palpitations, headache, trouble sleeping (if taken too late in the day), increased sweating, weight loss, dry mouth, nausea and stomach pain	Inattentiveness, excessive daytime sleepiness (EDS) and tiredness	It is a controlled substance, therefore increased medical supervision is required
Modafinil (Provigil)				
100 or 200 mg tablets	200 mg once/day in the morning	Headache, nausea, dizziness, trouble sleeping, anxiety, diarrhea, dry mouth	Same as above	Same as above

For more information about sleep and PD, visit Parkinson.org/Library to read or listen to *Sleep: A Mind Guide to Parkinson's* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Postural Low Blood Pressure

The terms postural low blood pressure, orthostatic hypotension (OH) and orthostasis can all be used to describe a drop in blood pressure that occurs when a person stands up. Blood pressure normally drops when a person stands up, but the body's autonomic nervous system keeps it within an acceptable range. Parkinson's can impact the reflexes that protect against this blood pressure drop. This results in lightheadedness, dizziness and fainting — typically within one to three minutes after standing.

Since the autonomic nervous system is often damaged in PD, automatic functions, such as blood pressure regulation, digestive system movements and sweating, can be affected. When OH is related to a nervous system disease, such as Parkinson's, it is also called neurogenic orthostatic hypotension (nOH).

Though it can be easy to assume new symptoms are connected to PD, other medical issues related to the heart or lungs can impact blood pressure control. These must be ruled out first. PD medications can also cause low blood pressure, especially dopamine agonists, amantadine and carbidopa/levodopa. Other prescribed medications, particularly those used to treat high blood pressure, should be closely reviewed.

People with Parkinson's can experience multiple health challenges at the same time. If you experience symptoms of low blood pressure, inform all members of your care team.

✓ TIP

People with Parkinson's may have low or normal blood pressure while standing and high blood pressure while sitting or lying down. For this reason, it may be beneficial to check blood pressure in three positions (lying down, seated and standing).

Non-Medication Treatments for OH

If you experience OH, your doctor may consider decreasing the dosages of certain PD medications that can cause this problem. If you are taking medication for high blood pressure, your doctor may reduce the size or frequency of doses or eliminate the medication altogether.

Medications are not the only way to manage OH. The following non-medication techniques are also important:

- Change positions slowly, particularly when rising from a seated to standing position. Pause for several seconds between each move. Walking with an assistive device (cane or walker) may also be helpful.
- Do simple exercises, such as raising your knees 10 times before standing and crossing your legs for 30 seconds after standing.
- Increase fluids, salt and caffeine in the diet, if this is safe for you.
- Wear graduated compression socks or stockings and elevate your legs periodically during the day. Compression garments can help improve circulation and maintain blood pressure; your doctor or pharmacist can help identify the amount of compression that's right for you.

Medications for Orthostatic Hypotension

If non-medication options do not help, your doctor may recommend a medication for increasing blood pressure. There are several options, which can be used on their own or in combination with other OH medications.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Droxidopa (Northera)				
100, 200 or 300 mg capsules	100-600 mg 3 times/day	Risk of high blood pressure when lying flat, nausea, headache and dizziness	Orthostatic hypotension (postural low blood pressure)	Last dose should be taken 3-4 hours before bedtime to reduce blood pressure increase risk

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Fludrocortisone (Florinef)				
0.1 mg tablets	0.1 mg once/day	Leg swelling, risk of high blood pressure when lying flat and low potassium	Orthostatic hypotension (postural low blood pressure)	Last dose should be taken 3-4 hours before bedtime to reduce blood pressure increase risk
Midodrine (Proamatine)				
2.5, 5 or 10 mg tablets	2.5-10 mg every 8 hours	Risk of high blood pressure when lying flat, itchy scalp, urinary retention and headache	Same as above	Same as above
Pyridostigmine (Mestinon)				
30 mg tablets	30 mg-60 mg twice/day	Nausea, diarrhea, urinary urgency, excessive sweating, excessive drooling, muscle twitching	Same as above	Same as above

For more information about low blood pressure, visit Parkinson.org/Library to read our fact sheet *Low Blood Pressure and PD* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Gastrointestinal Symptoms

Parkinson's affects the autonomic nervous system, which controls the normal movements of the gastrointestinal (GI) tract. In PD, normal stomach contractions slow down and everything that is swallowed — including medications — stays in the stomach longer than it should due to delayed emptying. Slowed stomach emptying can cause gas, bloating, nausea, loss of appetite and pain.

Nausea, constipation and feeling full or bloated after eating less than a full meal are common problems throughout the course of Parkinson's. Constipation occurs early in the evolution of PD, and it may increase in severity and frequency as Parkinson's progresses.

Medications for Nausea and Vomiting

The management of GI disorders in PD can be complicated. For instance, many Parkinson's medications can worsen nausea. The addition of extra carbidopa (Lodosyn) to carbidopa/levodopa (Sinemet) can help. However, giving additional carbidopa does not reduce nausea when it is caused by dopamine agonists, since carbidopa is only effective in the presence of levodopa.

NOTE

Other medications, specifically metoclopramide (Reglan), prochlorperazine (Compazine) and promethazine (Phenergan), are often used to treat nausea and vomiting. However, because they block dopamine, they can worsen PD symptoms and should be avoided.

Over-the-counter remedies, such as antacids, ginger capsules or ginger tea may provide some nausea relief. In addition, there are several medications that can be used to manage nausea and vomiting without worsening PD symptoms.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Carbidopa (Lodosyn)				
25 mg tablets	25-50 mg added to each dose of carbidopa/levodopa	Could worsen dyskinesia	Nausea and vomiting	Only treats nausea caused by levodopa therapy
Domperidone (Motilium)				
10 mg tablets	10 mg up to 3 times/day prior to meals	Headache, hives, hot flashes and dry eyes	Nausea, vomiting and constipation	Not available in the United States
Ondansetron (Zofran)				
4 or 8 mg tablets	4-8 mg up to 3 times/day as needed	Headache, tiredness, constipation and diarrhea	Nausea and vomiting	Should not be combined with apomorphine

Non-Medication Treatments for Constipation

Constipation is one of the most common PD non-movement symptoms. Fortunately, a high fiber diet and stool softeners, laxatives and other medications (as needed) are usually helpful. A combination of treatment strategies is most effective in treating constipation in PD:

- Drink plenty of water and fluids.
- Get regular exercise.
- Include lots of fiber in your diet by eating fruits, vegetables and bran cereals.
- Use fiber additives, such as psyllium fiber (Metamucil). Talk to your doctor about which additive or combination of additives is right for you.

Medications for Constipation

There are several medications for constipation. These are often combined with other treatment strategies. Guidance from your neurologist, primary care doctor or healthcare provider on how to use and combine these treatment options is essential.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
Lubiprostone (Amitiza)				
8 or 24 mcg capsules	8-24 mcg twice/day	Nausea, bloating, gas, dizziness and chest pain	Constipation	Works by increasing fluid in the intestines
Polyethylene glycol (Miralax)				
1 capful (17 g) in 4-8 oz water	Once/day as needed, may use lower doses for maintenance	Bloating, gas, diarrhea, nausea and abdominal pain	Same as above	Available over the counter

For more information about gastrointestinal symptoms, visit [Parkinson.org/Library](https://www.parkinson.org/Library) to read our fact sheet *Constipation and Other Gastrointestinal Problems in Parkinson's Disease* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Urinary Symptoms

Frequent urination (urinary frequency), feeling a strong need to go to the bathroom (urinary urgency) and loss of bladder control (urge incontinence) are common challenges in Parkinson's. In people with PD, the bladder loses its ability to hold normal amounts of urine because the brain gives messages to empty the bladder much sooner than physically necessary.

Urinary frequency and urgency can lead to incontinence (urine leakage). Movement fluctuations can also make it difficult to get to a toilet quickly when there is a sudden need to go to the bathroom. As with other non-movement symptoms, it is important to rule out other possible

causes of urinary frequency, including urinary tract infection, and for men, an enlarged prostate. It is important to consult a urologist (bladder and urinary specialist) and women can also consider a urogynecologist (pelvic floor specialists).

Medications for Bladder Control

A variety of prescription medications can help address urinary symptoms. Anticholinergic and beta-3 agonist medications are used to decrease urinary frequency, urgency and incontinence, while alpha blockers address symptoms caused by an enlarged prostate.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
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Anticholinergic Medications

Solifenacin (VESIcare)				
5 or 10 mg tablets	5-10 mg once/day	Dry mouth, constipation and dry eyes	Overactive bladder	Older adults may be more sensitive to anticholinergic medication side effects
Tolterodine (Detrol)				
1 or 2 mg tablets Longer-acting form also available	2 mg twice/day	Dry mouth, constipation, dizziness and drowsiness	Same as above	Same as above

Beta-3 Agonist Medications

Mirabegron (Myrbetriq)				
25 or 50 mg extended-release tablets	25-50 mg once/day	High blood pressure and headache	Same as above	Does not have anticholinergic side effects
Vibegron (Gemtesa)				
75 mg tablet	75 mg once/day	Headache, UTI, nasal congestion, diarrhea, nausea, upper respiratory tract infection	Overactive bladder	Does not have anticholinergic side effects

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
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Alpha Blocker Medications

Tamsulosin (Flomax)				
0.4 mg ER tablets	0.4-0.8 mg once/day with a meal	Low blood pressure, dizziness, headache, ejaculation failure and runny nose	Difficulty urinating due to enlarged prostate (benign prostatic hyperplasia [BPH])	Useful in the case of an enlarged prostate
Terazosin (Hytrin)				
1, 2, 5 or 10 mg tablets	1-10 mg once/day at bedtime	Low blood pressure, dizziness and swelling	Same as above	Same as above

For more information about urinary problems, visit [Parkinson.org/Library](https://www.parkinson.org/Library) to read our fact sheet *Urinary Problems in Parkinson's Disease* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Drooling (Sialorrhea)

Many things slow down in Parkinson's, including the automatic swallowing reflex that helps clear saliva from the mouth. Drooling can occur when excess saliva begins to collect. This can be a troubling issue for people if saliva escapes frequently, causing wet and sometimes irritated skin, damp clothing and even a wet floor. Severe drooling is often related to more serious swallowing difficulties (also known as dysphagia), which can cause choking when eating and drinking or lead to aspiration pneumonia (an infection when food or liquid gets into the airways or lungs).

Working with a speech therapist can help improve swallowing, manage drooling and reduce the risk of aspiration pneumonia.

NOTE

Speech, swallowing and drooling are non-movement symptoms, although they are mainly caused by decreased coordination of the muscles of the mouth and throat.

Drooling Medications

If lifestyle strategies are not effective, there are prescription medications that may help manage drooling by decreasing saliva production. These medications should be used with caution, as they can lead to dry mouth, which can increase tooth decay and impact overall oral health.

Formulations	Typical Treatment	Common Side Effects	Usage in Parkinson's	Special Considerations
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Anticholinergic Medications

Glycopyrrolate (Glycate)				
1, 1.5 or 2 mg tablets	1-2 mg 2 or 3 times/day as needed	Drowsiness, confusion, dizziness, blurred vision, constipation, flushing, headache and urinary retention	Decreases saliva production to address drooling	Although not FDA-approved for drooling, can decrease saliva production as a side effect
Glycopyrrolate oral solution (Cuvposa)				
1 mg/ 5 mL solution	1.5-3 mg 3 times/day	Dry mouth, vomiting, constipation, flushing and nasal congestion	Same as above	Same as above
Ipratropium bromide nasal spray (Atrovent)				
0.03% or 0.06% metered spray	1-2 metered spray under the tongue every 6 hours	Dry mouth	Decreases saliva production to address drooling	Although not FDA-approved for drooling, can decrease saliva production as a side effect
1% atropine eye drops (Isopto-Atropine)				
1% ophthalmic solution	1-2 drops under the tongue twice/day	Dry mouth	Same as above	Same as above

Botulinum Toxin Medications

There are several botulinum toxins that can be injected into the salivary glands in the cheek and jaw area to reduce saliva production. Incobotulinum toxin A (Xeomin) and rimabotulinum toxin B (Myobloc) are FDA-approved for excess saliva and drooling. Onabotulinum toxin A (Botox) and abobotulinum toxin A (Dysport) are used off-label (not FDA-approved for a specific condition) to decrease saliva production. Although botulinum toxin can be effective for drooling, it is costly, so doctors may recommend other treatments first.

For more information about drooling, visit [Parkinson.org/Drooling](https://www.parkinson.org/Drooling) or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Sexual Dysfunction

Common in PD, sexual dysfunction includes decreased sex drive, issues around sexual performance and uncontrolled sexual urges (hypersexuality). It is often undiagnosed partly because discussing sexual issues can feel like a taboo topic.

Movement and non-movement symptoms as well as PD medications can impact sexual performance and pleasure in Parkinson's. For example, decreased facial expressiveness (facial masking) and voice changes can interfere with non-verbal communication, an important part of intimacy. Depression can decrease sexual desire and some antidepressants can affect physical and emotional responses during sex.

✓ TIP

If there are times of the day when you feel and move better — for example when you are rested and medications are working well — this could be a good time to approach sexual intimacy with your partner.

In Parkinson's, sexual dysfunction may be related to loss of dopamine in the brain, which is responsible for delivering reward and pleasure. As with other non-movement symptoms, your doctor or another member of your healthcare team should consider non-PD-related issues that could impact sexual performance or decrease sex drive. These may include poor circulation to the genitals, which commonly occurs in diabetes and peripheral vascular disease, enlarged prostate, depression and other medical conditions.

Many medications, including some antidepressants and drugs for high blood pressure as well as excessive alcohol or tobacco use, can impact sexual performance or decrease sex drive. Fortunately, most PD drugs are not associated with sexual dysfunction in this way, with the exception of anticholinergics. In fact, dopamine agonists have been associated with impulse control disorders, including uncontrolled sexual urges (hypersexuality).

Treatments for Sexual Dysfunction

Discuss any issues related to sexual performance and sex drive with a member of your healthcare team, who can recommend the best treatments to help manage your

symptoms. In addition to your Parkinson's doctor, other healthcare team members can help with addressing sexual health, including a psychologist, nurse, primary care doctor or a gynecologist for women or urologist for men. Working with a sex therapist or couples' therapist can also be helpful.

Depending on a person's needs, a variety of oral, topical and injectable medications as well as assistive devices are available to help people experiencing sexual function issues. Symptom management varies depending on the type of issue a person is experiencing. For example, bupropion (Wellbutrin SR) may improve sexual function issues related to SSRIs — a class of antidepressants. Flibanserin (Addyi), which affects the levels of serotonin, dopamine and norepinephrine in certain parts of the brain, is FDA-approved for female sexual dysfunction in premenopausal women. In postmenopausal women with hypoactive sexual desire disorder (persistent decrease in sex drive), topical hormone therapy may be beneficial.

Although a detailed review of sexual dysfunction in PD and its treatment is beyond the scope of this book, one of the most common sexual complaints — erectile dysfunction — is briefly discussed below.

Non-Medication Treatments for Erectile Dysfunction

There are a variety of treatment options for erectile dysfunction. Exercise, weight loss and management of other medical conditions, such as depression, diabetes and sleep apnea, can improve symptoms. Vacuum pumps, constriction rings and penile implants are also available.

Medications for Erectile Dysfunction

Oral medications for erectile dysfunction include the phosphodiesterase-5 (PDE5) inhibitors sildenafil (Viagra), vardenafil (Levitra) and tadalafil (Cialis). Flushing and headache are common side effects. People taking nitrate medications, such as nitroglycerin, isosorbide mononitrate and isosorbide dinitrate, should not use PDE5 inhibitors due to the risk for severe hypotension. Injectable medications include papaverine (papaverine vials for injection) and phentolamine (Regitine vials for injection). Either the person with PD or a care partner injects this medication directly into the penis. Unique drug combinations can be made by a pharmacy. For example, TriMix is a combination of papaverine, phentolamine and alprostadil (prostaglandin E1). This approach may help lower costs and allow for more precise dosing. Pain or scarring of the penis may result. Priapism, an erection that lasts more than 4-6 hours, is considered a medical emergency.

Other injectable medications include alprostadil (Caverject), which is instead injected into the urethra (the opening at the tip of the penis). This approach can cause bleeding and pain in or around the injection site; it is also less effective than penile injections.

For information about intimacy, visit [Parkinson.org/Library](https://www.parkinson.org/Library) to read our fact sheet *Intimacy and PD* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

Seborrheic Dermatitis

Many people with Parkinson's will develop skin-related symptoms, including seborrheic dermatitis. Seborrheic dermatitis, which affects about 50% of people with PD, is a condition that causes oily, red, flaky, itchy and/or scaly skin, commonly around the scalp and face.

Seborrheic dermatitis develops when oil-producing skin glands become infected with a particular yeast. It is not contagious. Stress, hormone changes, the use of alcohol-based skin products and cold, dry air may worsen symptoms. Difficulty regulating body temperature, an autonomic issue that some people with PD experience, may also contribute to the development of seborrheic dermatitis.

Treatments for Seborrheic Dermatitis

Although there is no cure for seborrheic dermatitis, topical antifungals and topical anti-inflammatory drugs, such as corticosteroids and topical calcineurin inhibitors, are commonly used to manage symptoms.

The type of treatment selected is based on the location and severity of symptoms. Over-the-counter antifungal dandruff shampoos and creams can often manage mild seborrheic dermatitis. Ketoconazole 2% and ciclopirox 1% are both available in shampoo and cream form by prescription only. Facial hair may also require treatment with an antifungal shampoo.

Topical corticosteroids, such as hydrocortisone and betamethasone, can be used alone or in combination with antifungal medications. While topical antifungals and anti-inflammatory drugs are generally safe, using a topical corticosteroid every day for several weeks can lead to thinning skin or red or pink lines or patches on the skin. Topical calcineurin inhibitors, such as pimecrolimus 1% or tacrolimus 0.1%, may be substituted for people who frequently require corticosteroid therapy to reduce these risks.

Discuss non-medication, over-the-counter and prescription treatment options with your doctor or pharmacist. Your doctor may refer you to a dermatologist.

Excessive Sweating

More than 50% of people with Parkinson's experience excessive sweating, which consists of sudden, drenching sweating of the head and neck. This can be caused by body temperature regulations issues, common in PD.

Some people notice that they sweat large amounts during "off" periods when symptoms worsen or when dyskinesia is severe enough to increase body temperature. Many people report sudden and unexplained drenching sweat, often awakening them from sleep and soaking the bed sheets. Carbidopa/levodopa can also cause severe episodes of sweating.

Treatments for Temperature Regulation Symptoms

When related to movement fluctuations or dyskinesia, adjusting PD medications to improve symptom control can improve temperature regulation.

NOTE

If you are taking anticholinergic medications, which help block sweat secretion, your Parkinson's doctor may consider reducing or eliminating these drugs, especially in warmer weather, as they can contribute to overheating.

Prescription antiperspirants, topical anticholinergics, botulinum toxins and certain medical devices may also be used to combat excessive sweating. Wear loose-fitting clothing, use armpit shields or garment guards and avoid foods or activities that trigger sweating to help reduce anxiety or discomfort related to excessive sweating.

Pain

About 66% of people with Parkinson's report experiencing pain. It is important to identify the source and type of pain whenever possible to help guide your treatment plan.

Other painful conditions may coexist with PD, including arthritis, peripheral neuropathy, spinal stenosis, a pinched nerve in your spine, and musculoskeletal strains and sprains. These alternative causes of discomfort should always be considered before assuming pain is due to Parkinson's.

The most common cause of pain from PD is dystonia, sustained contractions leading to abnormal postures of the neck, arms, legs or feet. Depending on the timing of the pain and location, multiple approaches may be helpful. Early morning dystonia often improves with movement or the first dose of a Parkinson's medication. In some cases, people with severe morning dystonia use a fast-acting rescue medication. If dystonia occurs as a medication wearing-off symptom, minimizing the "off" period with medication adjustments or deep brain stimulation can be beneficial. Botulinum toxin injections can also be helpful in treating dystonia that affects a single body region.

Musculoskeletal pain may be related to rigidity and decreased movement or mobility. If you are experiencing this kind of pain, physical therapy and PD medication adjustments can help.

Depression, which is common in PD, can heighten the experience of pain. This highlights the importance of identifying and treating depression in Parkinson's disease.

Approaches to Pain Management

Management of chronic pain in Parkinson's can be challenging. Treatment plans should be individualized and include a combination of medication and non-medication therapies. Many

non-medication therapies have been proven effective for managing pain, including regular exercise, heating pads, ice packs and massage. Although we often think of medications as a solution for new symptoms, pain is unique in that non-medication options can often make the biggest difference.

Medications for Pain Management

Acetaminophen (Tylenol) is commonly used for many different types of pain. Work with your doctor to find the right dose for you, as high doses can contribute to liver damage. Acetaminophen is commonly formulated in combination with other drugs, ranging from over-the-counter cough/cold remedies to prescription pain medications. For this reason, it is important to check all medication labels and add up the total amount of acetaminophen being taken from all sources.

Anti-inflammatory medications include steroids and non-steroidal anti-inflammatory drugs (NSAIDs). These are available both over-the-counter and by prescription and can help with musculoskeletal pain. Common NSAIDs include ibuprofen (Advil, Motrin), naproxen (Aleve) and diclofenac (Voltaren). Oral NSAIDs should be taken with food to minimize GI upset. Common side effects include nausea, stomach ulcers and swelling or fluid retention. Steroids can have similar side effects to NSAIDs; however, long-term steroid use can cause other issues such as high blood sugar and bone loss.

Muscle relaxants are sometimes used for muscle spasms but are not typically considered a long-term solution for pain, as they can cause dizziness, drowsiness, confusion and low blood pressure and lead to falls. Common muscle relaxants that have been shown to be effective for spasms include cyclobenzaprine (Flexeril), tizanidine (Zanaflex) and baclofen.

If pain is thought to be related to nerves, medications such as serotonin and norepinephrine reuptake inhibitors and tricyclic antidepressants or antiseizure drugs (gabapentin [Neurontin] and pregabalin [Lyrica]) may be used. Gabapentin and pregabalin must be increased gradually over several weeks to minimize side effects while working up to an effective dose. Common side effects include dizziness, sleepiness, blurry vision and walking changes.

Opioid medications such as tramadol (Ultram) or oxycodone (Oxycontin) are sometimes used short-term after an accident or surgery or for various types of pain, including nerve pain, if other options have failed. Side effects include drowsiness, confusion, constipation and decreased breathing. Opioid medications can lose their effect over time, requiring higher doses and increasing the risk of serious side effects. Even at doses commonly prescribed, opioids can be addictive, which can lead to serious injury, accidental overdose and death. If you are taking an opioid, talk to your doctor or pharmacist about getting a "rescue" medication called naloxone (Narcan), which can be administered by a bystander or care partner in the event of an overdose.

Involving Your Healthcare Team

When pain lasts longer than two weeks, interferes with sleep or intensifies, it is time to involve

your team. Keep track of **when** the pain started, **where** it hurts, **how** long it lasts and **what** it feels like — for example, burning, achy, sharp.

It is useful to track when the pain starts in relation to when you take your medication. This information will help your healthcare team work more efficiently with you in designing a treatment plan. Your doctor may refer you to a pain specialist.

Even with treatment, becoming "pain-free" may not be realistic; however, working with your healthcare team to identify the medications and therapies that work best for you can often help reduce pain and improve everyday life.

For more information about urinary problems, visit [Parkinson.org/Library](https://www.parkinson.org/Library) to read our fact sheet *Pain and PD* or call our Helpline at **1-800-4PD-INFO (1-800-473-4636)**.

4 Development of New Drugs

Researchers are working to target breakthroughs that can slow and stop Parkinson's disease (PD) progression.

New research is investigating opportunities in several areas:

- ▶ Preventing Parkinson's
- ▶ Slowing disease progression
- ▶ Diagnosing Parkinson's and measuring progression
- ▶ Replacing or restoring lost function (neurorehabilitation)
- ▶ New symptomatic treatments, such as continuous subcutaneous (under the skin) therapies
- ▶ The role of exercise

You can help scientists advance research by participating in studies to find new treatments and improve quality of life for people with Parkinson's.

Drugs and devices must go through a clinical trial process before the U.S. Food and Drug Administration (FDA) can consider approving a new therapy. A clinical trial is research conducted with people to answer scientific questions. Clinical trials determine if scientific concepts can be turned into safe and effective therapies that make life better for people with Parkinson's.

The entire process of bringing a new medication to the pharmacy can take up to 10 years from the time it is tested in a laboratory to the time it can be prescribed as a treatment.

There are four clinical trial research phases for drug and device studies:

Phase I

Tests potential treatment for the first time in a small group of people (usually healthy volunteers) to evaluate safety, determine the safe dosage and identify side effects.

Phase II

Further evaluates the safety of the treatment being tested and provides preliminary measures of effectiveness in people with the disease of interest.

Phase III

Determines if the treatment benefits participants and if the benefits outweigh the risks by testing it in large numbers of people (usually hundreds).

Phase IV

Involves collecting and reviewing additional information about a treatment – including risks, benefits and optimal use – after it has been approved for use by the FDA.

Read about how to evaluate research studies in Appendix C on page 57.

For more information about our research initiatives and how to become an advocate, visit [Parkinson.org/Research](https://parkinson.org/Research). View or download our fact sheet *Getting Involved in Research* at [Parkinson.org/Library](https://parkinson.org/Library) to learn about participating in studies.

You can also contact our Helpline at **1-800-4PD-INFO (1-800-473-4636)** or Helpline@Parkinson.org for help finding a clinical trial near you.

Appendix A

Managing "Off" Time

In early Parkinson's disease (PD), medication can work smoothly to control movement symptoms, and daily life typically continues as normal for many people. As time goes on, symptom management becomes more challenging, which means you may need to explore different medication combinations and treatment strategies with your doctor to continue living your best life.

Understanding Dopamine and Parkinson's

The nervous system is made up of nerve cells (neurons) that form a "communication network" within the brain and throughout the body. Neurons in a part of the brain called the substantia nigra produce dopamine, a chemical messenger (neurotransmitter) essential for smooth, controlled movement. In Parkinson's disease, these neurons stop functioning normally and die. Levodopa, the main ingredient of the medication carbidopa/levodopa (Sinemet), converts into dopamine in the brain, which helps restore movement function in people with PD. Dopamine agonists work by mimicking dopamine.

Medication Complications

Levodopa medication can be used throughout the course of PD; however, as Parkinson's progresses, the brain gradually loses some of its ability to store and use dopamine effectively. As a result, people taking carbidopa/levodopa — typically those who have been taking it for a while — often experience a wearing-off effect, or a return of symptoms in between medication doses. Symptoms may return gradually or suddenly, like flipping a switch. After taking the next dose, symptoms usually improve, and people feel "on" again. This phenomenon, known as "on/off" fluctuations, may also occur when taking dopamine agonists but to a lesser degree.

For some people, the combination of brain changes and levodopa therapy can lead to dyskinesia (uncontrolled, involuntary movements). Other people may never develop dyskinesia. Levodopa therapy can also cause painful muscle contractions (dystonia), fatigue, hallucinations, delusions and low blood pressure. Balancing symptom relief with medication side effects becomes complex, often requiring the expertise of a neurologist with special training in movement disorders, known as a movement disorder specialist.

"On/Off" Fluctuation Symptoms and Timing

As with PD symptoms, each person experiences "off" episodes differently. One person may have more slowness (bradykinesia), stiffness (rigidity) or tremor as medications wear off. Freezing and muscle contractions (dystonia) can also be wearing-off symptoms. In fact, any symptom that improves with carbidopa/levodopa therapy can worsen or intensify when medication wears off, including non-movement symptoms like anxiety, depression, fatigue, foggy thinking and pain.

"On/off" fluctuations, though more common at the end of a dose cycle, can happen at any time during the day or night.

You may experience just one or a combination of the following "off" situations:

- Early morning "off" when you wake up and your morning dose of medication has not started to work
- Middle of the night "off" episodes after the evening dose wears off
- End-of-dose "off," which usually happens before the next dose is taken
- A sudden, unexpected "off" not related to the timing of the medication
- An "off" episode following a large or protein-rich meal. Protein can delay or stop levodopa's effects.
- Delayed "on" while waiting for the medication to start working. This usually occurs due to delayed stomach emptying.
- Dose failure when a single dose of carbidopa/levodopa does not provide its usual benefit

Treatment for "On/Off" Fluctuations

Treatment for "on/off" fluctuations is individualized. Your doctor will adjust your medications while watching for new or increased medication side effects. Depending on your current medications, your doctor may:

- Adjust the frequency or dose size of your levodopa medication.
- Use extended-release or quick-acting dopaminergic medications.
- Add different medications to keep dopamine levels more consistent.
 - Catechol-O-methyltransferase (COMT) inhibitors can extend levodopa benefits.
 - Monoamine oxidase-B (MAO-B) inhibitors promote dopamine.
 - Adenosine A2a antagonists can extend "on" time.
 - Dopamine agonists may help carbidopa/levodopa last longer and smooth out the "on/off" effect.
 - Amantadine ER (Gocovri) treats "off" episodes and dyskinesia.

If these medication adjustments cause or increase dyskinesia, adding an amantadine formulation may help.

Appendix B

Formula for Liquid Sinemet

Formula for Liquid Sinemet (1 mg levodopa per 1 mL solution)

Ingredients:

- Sinemet 25/100 immediate-release tablets: 10 tablets (1,000 mg levodopa) (do not use controlled or extended-release formulations)
- Ascorbic acid (Vitamin C) crystals: 1/2 teaspoon (approximately 2 grams)
- Tap water or distilled water: 1 liter or quart

Directions:

1. **Mix the above ingredients** in a liter/quart plastic container with lid (do not use metal).
2. **Rotate or shake gently until tablets dissolve** (no need to crush tablets). Tablets may not go completely into solution.

Formula will maintain full strength and purity for 24 to 48 hours in refrigerator.

Dosing Recommendations

Always establish a dosing plan with your physician or healthcare provider first!

1. Morning "jump start" dose:

- 60 mL of the formula (60 mg or a little more than 1/2 of a 25/100 tablet of carbidopa/levodopa) or may use amount comparable to usual tablet dose.
- Adjust dose 5-10 mL up or down every three to five days until you achieve the best "on" response with the least dyskinesia.

2. Hourly dosing:

- 30 mL of the formula on the hour while awake, or hourly proportion of usual tablet dose. (For instance, a person taking one carbidopa/levodopa 25/100 tablet every two hours might try 50 mL per hour of the liquid.)
- Adjust dose 5-10 mL up or down every three to five days until "on" periods are smoother.

✓ TIPS

For the best result, adjust the morning jump-start dose prior to adjusting the hourly doses. Accuracy of the dose and exact hourly timing between doses is critical for best results.

Appendix C

Evaluating Research Studies

New drugs and other Parkinson's disease (PD) treatments often gain attention through popular media. Companies with shareholders must report study results as soon as they are available and before they are presented at scientific meetings. This is usually done in the form of a press release. While headlines may make it sound like new drugs are available, a closer look often reveals that the new drug is only in the early stages of research and years away from becoming an available treatment. Taking some time to evaluate the research behind the headlines can help determine the best way to use the new information.

Below are some questions to ask when evaluating clinical studies of new medications and treatments for PD:

- What is the source of the information? Has the information been published or presented at a trustworthy scientific meeting, or is the information from unscientific and possibly incorrect resources? Check with a member of your healthcare team to determine if the source is reliable.
- How many people participated in the study? The higher the number of participants, the more likely the results will achieve statistical significance and accuracy.
- How was the study designed? The benchmark for the most valid clinical trial is one that includes all of three elements:
 1. Participants are randomized to equal treatment groups
 2. Is double-blind (researchers and participants are both unaware of which treatment each participant receives until after results are tallied)
 3. Includes a placebo group (participants who receive a "fake" treatment such as a sugar pill)

Appendix D

Medication and Hospitalization

People with Parkinson's often have complex, individualized and precisely timed medication regimens. This can be difficult to maintain in the hospital setting for a variety of reasons:

- Nurses distribute medications on set schedules. For most medications, the window of delivery is an hour before the scheduled medication time to an hour after. Nurses may not realize that a 15-minute delay could impact your ability to move.
- Hospital pharmacies may not keep your specific PD medications in stock.
- Some commonly used medications in the hospital can worsen PD symptoms.

To help your hospital healthcare team understand, the following steps are important:

- Advocate for yourself or select a trusted care partner or family member to advocate for you.
- Provide a list of all the medications you take along with the amounts and times you take them. Double check this information is accurate in your hospital medical chart.
- Ask if the hospital pharmacy stocks your specific medications. If not, request to use your own. A letter from your doctor explaining the need for your own medications may be required for hospital staff to allow their use.
- Emphasize that delaying or stopping PD medications will not only affect your symptoms but can also be dangerous.

✓ TIPS

Keep a set of your medications in their original bottles to make taking your own medications in the hospital possible.

The Parkinson's Foundation Hospital Safety Guide contains information to give to hospital providers about Parkinson's and what medications are safe for people with PD. Download or order a Parkinson's Foundation Hospital Safety Guide online at [Parkinson.org/HospitalSafety](https://parkinson.org/HospitalSafety).

About the Parkinson's Foundation

The Parkinson's Foundation makes life better for people with Parkinson's disease by improving care and advancing research toward a cure.

In everything we do, we build on the energy, experience and passion of our global Parkinson's community. Information about Parkinson's and resources are available at, [Parkinson.org](https://parkinson.org).

Your generosity makes this publication possible.

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