Moving Forward™
3rd Edition

A practical guide to living with Parkinson’s disease
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A practical guide to living with Parkinson’s disease

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About this guide
The face of Parkinson’s disease (PD) has changed tremendously in the past few decades, and PD experts see many reasons for hope in the coming years. As we learn more about the disease, develop better treatments, and continue the search for a cure, the future looks bright.

Today, more than ever, there are things you and your loved ones can do to help improve the quality of your life and manage the effects of Parkinson’s disease. Becoming actively involved in your own treatment and care is one of the best things you can do to manage your PD.

The first step you can take to help manage your PD is to arm yourself with knowledge about the disease and your treatment options: learn about PD therapies that might meet both your lifestyle and treatment needs. Then, be prepared to discuss your needs and preferences with your family, doctors, and nurses as you work together to manage your PD.

As part of our commitment to helping people manage their PD, Teva Neuroscience, Inc. has developed Moving Forward™ to assist you in this process. Moving Forward™ offers information about different aspects of PD, as well as useful tips and resources. Teva also publishes Life in Balance, a newsletter for people and families living with PD that provides updates on the latest developments in PD; you can receive Life in Balance free of charge just by registering at www.parkinsonshealth.com. Together, Moving Forward™ and the Life in Balance newsletters offer comprehensive information about PD with encouragement, direction, and hope.

In developing these resources, Teva recognizes that PD affects each person differently. We know that the symptoms of PD do progress over time, and they do so at different rates in different people. That’s why this guide is intended as a general road map to point you in the direction of other helpful resources to meet your personal needs. If the information here does not meet your personal needs, talk to your doctor or nurse about additional resources to help you learn how to better manage your PD.

We hope you find Moving Forward™ to be a helpful tool that inspires you to make a lifelong commitment to taking an active role in the management of your PD.
The development of Moving Forward™ would not have been possible without the dedication of our advisory council. We thank them for sharing their time, knowledge, and passion with the PD community.

Participation of the consultants in the development of this book does not constitute an express or implied endorsement of any medications.

About the advisors

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Dr Elmer is the director of the Center for Neurological Health and the Parkinson’s Disease and Movement Disorder Program as well as professor in the Department of Neurology at the University of Toledo College of Medicine. Dr Elmer earned his MD and PhD at the University of Florida College of Medicine. He completed his medical internship at the Sioux Falls VA Medical Center and his neurology residency and fellowship training in movement disorders at the University of Michigan. He also completed postdoctorate work in the Department of Physiology and Molecular Biophysics at Baylor College of Medicine and at the Howard Hughes Medical Institute in Ann Arbor, Michigan.

**Suzanne Geffen Mintz, MS**

Ms Mintz is president and CEO of the National Family Caregivers Association (NFCA), an organization dedicated to fulfilling the unmet needs of family caregivers. Ms Mintz, a family caregiver herself for her husband, who has multiple sclerosis (MS), is widely recognized as a thought-leader and spokesperson for the caregiving community. She has testified before Congress and is frequently quoted by the media. Her latest book is *A Family Caregiver Speaks Up: “It Doesn’t Have to Be This Hard.”* She is also the author of numerous articles. Ms Mintz serves on the Governing Board of the National Patient Safety Foundation and the Advisory Task Force of the National Transitions of Care Coalition. In 2006, she was one of only 15 people in the country to receive the Purpose Prize, an award for social entrepreneurship.

**Claire Henchcliffe, MD, DPhil**

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in New York. Dr Henchcliffe earned her MD at the College of Physicians and Surgeons at Columbia University in New York, and her DPhil at the University of Oxford in the United Kingdom. She completed her medical internship and neurology residency at the Columbia Presbyterian Medical Center, New York-Presbyterian Hospital, and her clinical fellowship in movement disorders at the Center for Parkinson's Disease and Other Movement Disorders at the Neurological Institute, Columbia-Presbyterian Hospital. In addition, Dr Henchcliffe completed postdoctoral training at Cambridge University in the United Kingdom and at the University of California at Berkeley.

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Ms Wichmann is the manager of Struthers Parkinson’s Center in Minneapolis, Minnesota, and a core faculty member of the National Parkinson Foundation’s Allied Team Training for Parkinson program. She is a recognized speaker and author of several publications on physical therapy management in PD, and remains involved in numerous regional and national efforts designed to improve PD education and awareness for family care partners, long-term care facilities, and rural outreach areas. Ms Wichmann earned her bachelor’s degree in physical therapy at the University of Minnesota.

**Kathryn G. Whitford**

Ms Whitford is the associate executive director of the American Parkinson Disease Association, and the former executive officer of K. Grant Whitford Inc., a national and international award-winning marketing firm serving not-for-profit, corporate, and association clients for 25 years. She earned degrees from the University of Pittsburgh and Long Island University, as well as certifications in Healthcare Marketing and Healthcare Administration at New York University and in Healthcare Quality Assurance at Harvard University.

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Ms McClain is a nurse practitioner at the Parkinson’s Disease and Movement Disorders Center at the University of South Florida in Tampa; her areas of special interest include PD, restless leg syndrome, and clinical trials. She represents the Center at related support groups in the area and also conducts patient education programs locally in conjunction with the Tampa General Outreach program. Ms McClain earned her master’s degree in nursing at the University of Cincinnati.
I was diagnosed with Parkinson’s disease in June of 2000; it was like a great weight was lifted off my shoulders. It took 18 months, but once diagnosed, I sat down, took a look at my life, and decided I wanted to work on the quality of my life.

The decision to retire took some time, but once decided I went head long into doing all the things I wanted to do. In October 2003, I left the firm where I had worked for 43 years. Since that day, I have been knitting and crocheting afghans, sweaters, hats, stuffed toys, you name it. I discovered floral arranging, gardening, and tried my hand at numerous crafty projects. I also found the benefits of tai chi, aerobics, and stretch classes, as well. In fact, last year I participated in the Senior Olympics with my tai chi class and demonstrated the various poses. I have been invited back again.

I discovered the American Parkinson Disease Association and the Salvatore and Elena Esposito Information & Referral Center’s support group for Parkinson’s patients and their caregivers. I donate my time assisting the nurse/coordinator and help to create further awareness of Parkinson’s by attending health fairs, decorating bulletin boards, as well as volunteering at APDA.

I’m having the time of my life despite the Parkinson’s—or is it because of Parkinson’s disease?

Susan Ernst
Staten Island, New York
Introduction

Being diagnosed with Parkinson’s disease may feel overwhelming. Fortunately, there are many steps you can take to maintain an active, healthy life with PD, such as

- Empowering yourself with knowledge about PD
- Maintaining a positive attitude
- Partnering with your physicians
- Taking an active role in managing your health

By using these strategies, you can take control, manage your disease, and continue to do the things you enjoy as long as possible.

This guide was designed to help you actively manage your PD. It contains a large amount of information about PD, covering topics that range from current treatment options to advocacy organizations. It also provides insight into the roles of different people involved in the treatment and care of PD, including your family and friends, trained health care professionals, and patient advocacy organizations. With this knowledge, you can take an active, confident role in creating a team of support.

As you read through this guide, you will also find tips on where to turn for additional resources. Those resources, and the right information and counsel from your doctor, can make living with the challenges of PD much more manageable.

The language of PD sometimes can be difficult to understand, so you will find key terms defined in the Glossary beginning on page 81.

Many of the resources in this guide are Internet-based. If you do not have Internet access, check the Resources section starting on page 74 for phone numbers, or visit your local library or community center where free Internet access may be available.

Ultimately, it’s important for you to remember that PD does not define you and your life — you have the power to define how you live with your PD.
PD basics
Understanding PD

Movement and coordination in your body are controlled in part by a chemical in your brain called dopamine. This brain chemical is used to send messages to your muscles to make them move properly. PD is a disorder of the central nervous system caused by a lack of dopamine. In PD, dopamine-producing nerve cells are damaged, gradually reducing dopamine levels in the parts of the brain thought to control movement. The loss of dopamine causes a variety of movement problems.

Estimates suggest that as many as 1.5 million people in the United States have PD. The average age of onset is approximately 60 years, but estimates suggest up to 15% of people with PD may be diagnosed under the age of 40 years. The incidence of PD increases with age and affects slightly more men than women.

Although great progress has been made in understanding PD, the cause is still unknown. Many researchers believe that some combination of environmental and genetic factors contributes to the onset of PD.

The good news in all of this is that there are many effective therapies that have been developed in recent years to relieve many PD symptoms. Even now, new medications and approaches to PD treatment are being developed. These new therapies and a proactive management of PD not only make it possible to live longer with PD than before, they may also make it possible to help slow the progression of PD and its symptoms. Many people living with PD continue to work full- or part-time and enjoy the activities they love long after diagnosis.

Symptoms and progression

If you have PD, you may find that ordinary actions become more difficult—getting dressed or preparing a meal may not be as easy as it once was. Although symptoms can vary from person to person, your doctor will most likely look for some common ones to determine whether you have PD. Some symptoms that are frequently associated with PD include tremor of a hand or arm, stiffness, slowness, and/or loss of balance. Other seemingly unrelated symptoms may include depression or sleep disturbances (including acting out dreams while asleep), muscle cramping, soft speech or difficulty swallowing, and challenges in initiating or maintaining movement.
Because PD is a progressive illness, symptoms slowly worsen over time. However, the rate of changes and the types of symptoms experienced are different for every person with PD. As a result, you cannot make a true comparison between your symptoms and stage of PD and someone else’s experience with PD. It is most important to remember that there are many ways you can help yourself and stay active in your everyday life.

The table above lists symptoms that are often associated with PD. The symptoms may help you recognize issues to discuss with your doctor.

As of this writing, no laboratory or blood tests are available to diagnose PD. Sometimes doctors may have patients undergo brain scans or lab tests to rule out other diseases as the source of their symptoms. Further examination and tests may be needed to establish whether a patient has PD or another parkinsonian type of disease.

Genetic testing for PD is available, too. However, it is only helpful for a minority of patients who either carry a known mutation linked to PD or are at risk of PD due to a family history of the disease. In the meantime, new methods of screening for PD are under investigation and review.

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<table>
<thead>
<tr>
<th>PD SYMPTOMS*</th>
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<tr>
<td><strong>Movement related</strong></td>
</tr>
<tr>
<td>• Tremor in the limbs</td>
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<tr>
<td>• Impaired gait</td>
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<tr>
<td>• Stiffness, cramping</td>
</tr>
<tr>
<td>• Slowness</td>
</tr>
<tr>
<td>• Decreased arm swing on one side</td>
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<tr>
<td>• Small handwriting</td>
</tr>
<tr>
<td>• Changes in expression, such as slowness/weakness in voice, face, and gesture</td>
</tr>
<tr>
<td>• Problems with balance</td>
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*Some of these are not specific to PD and may be associated with other conditions or medications. All symptoms should be evaluated by a doctor.
I was diagnosed with PD on July 19, 2002. My first 2 years with the disease were some of the darkest, but one morning in December of 2004, I found myself wondering what the rest of my life would look like. The answer was really simple. I had to somehow find the strength to make the best of things and live my life to the fullest.

The first thing I did was decorate the outside of the house for the holidays. This was followed by a series of home improvement projects that included painting several rooms, installing shelves and molding, and remodeling my kitchen. With the help of friends, my house—and my outlook—continued to change as the year came to an end. Before I knew it spring had arrived, and I started to plant flowers. I also began oil painting and decided to do volunteer work for the American Parkinson Disease Association (APDA).

Today, I’m vice president of the Long Island chapter of the APDA. I try to stay as active as I can, but some days my body won’t allow it. That might be something I may never have control over again, but my attitude is another matter altogether. I have learned that having the right attitude, and a lot of faith, makes almost anything possible.

Lou DeCaro
Wading River, New York
Developing a game plan
Now that you’ve reviewed some basic information, you should have a better sense of how PD may affect different aspects of your life. This guide will help you take better control of your life with PD and create a strategy on how to handle it.

Managing PD can get complicated. There are so many PD-specific things to consider that it is easy to lose sight of your overall health. A game plan will help you approach your well-being holistically and provide structure to balance your PD management with your lifestyle and other personal needs.

Start by considering your personal priorities. Think about the things you value most in your daily life. These might include:

- Maximizing your independence
- Maintaining relationships with family and friends
- Continuing your work or hobbies
- Ensuring your emotional well-being
- Maintaining your activities of daily living
- Managing troublesome side effects
- Reducing your PD symptoms

Discuss your status and priorities with your family and health care team. Make sure you have detailed discussions about how you’re doing. Consider how your health-related decisions could impact your priorities. Seek treatments offering symptom management.

When you receive your diagnosis, consider seeking therapy to help compensate for any changes in your physical abilities, speaking voice, handwriting, or other issues that may impact your daily life. If you experience periodic depression, explore the tips in the Emotional well-being Chapter 7 and speak with your doctor about issues of depression. Commit to doing whatever you can to lessen the impact of issues that interfere with the things important to you. PD patient advocacy groups offer great information about these topics (see pages 75-76 for listings).
Developing a game plan

Have a heart-to-heart conversation with your family caregiver about his or her concerns and feelings. Your PD will affect him or her on a daily basis, and his or her opinion is important to consider. The two of you are a team that can be very effective when you both recognize one another’s concerns, feelings, and responsibilities.

### QUESTIONS TO CONSIDER

Your PD—and other aspects of your health—will change over time. Your approach to managing PD should change as well. Evaluate your overall disease management by asking yourself the following questions on a regular basis:

- What are my priorities now?
- Are my treatments effective for me?
- Do any medication side effects interfere with my daily life?
- Does the benefit from my treatments come and go?
- Has it become more difficult or impossible for me to enjoy or participate in activities that I value?
- Have my interactions with friends or family changed because of PD?

The answers to these questions should help you determine whether it is time to make changes in your approach to disease management. You may want to speak with your doctor about modifying your medications, adding complementary or alternative treatments, beginning physical therapy, or enlisting additional assistance with daily living skills. Identifying and focusing on what is most important to you will allow you to manage PD without allowing it to control your life.
Working with your medical team

Your medical team may include your primary care physician or internist, as well as a neurologist. You may also find it helpful to have the support of a physician’s assistant or nursing specialist, such as a neurological nurse or nurse practitioner.

The important role of a specialist

PD is a very complicated disorder. Symptoms vary from person to person and mimic symptoms of numerous other diseases, making accurate diagnosis difficult in some people. For that reason, people living with PD may want to consider consulting with a neurologist or movement disorder specialist. In particular, a movement disorder specialist may be helpful if you’re not satisfied with your treatment or if your PD symptoms seem unmanageable.

If you’re happy with your PD status and treatment, then it’s fine to keep seeing the physician who is helping you manage your PD. However, you may have been referred to a specialist by your primary care physician based on early symptoms of PD. If you are not currently working with a specialist, you should talk to your primary care physician about getting a referral.

Choosing a specialist

Base your selection of a PD specialist on research, referrals, and an understanding of your own personal needs. You may not necessarily work with the first specialist you see. Make sure you find someone with whom you are comfortable. Your PD specialist will be an important part of your life for many years, and investing in the process of finding someone you like and trust will pay off over time.

Where to find a specialist

When it comes to identifying potential specialists, there are several sources you can turn to for help:

- Ask your primary care physician for referrals. He or she should be able to provide the names of several specialists

- Contact your insurance provider for a list of neurologists or movement disorder specialists within your network. If your network does not include neurologists or movement disorder specialists, request information about working with someone out of network
• Seek referrals from others living with PD. This is one of many reasons support groups are an important resource

• Consult PD advocacy groups (see pages 75-76 for listings). Many list PD specialists by state

**Managing treatment with multiple doctors**

Although our medical system generally offers the flexibility of working with several doctors to best meet your health care needs, it does not ensure that information from one of your doctors will be provided to another. That responsibility therefore falls to you and your family caregiver.

Coordinating your health care is one of the most critical things you can do to ensure safe and quality medical treatment. You should provide copies of your personal medical information to each physician involved in any treatment decision for PD or other conditions. It is essential to share medication information with all the doctors involved in your care so that treatment for one condition does not interfere or interact with treatment for another.

As your life with PD evolves, keep in mind that medications—like other types of PD therapies—are designed to improve your symptoms. If your medication does not provide any improvement, or the effects seem to decrease, let your doctor know.

The Internet offers some helpful tools for compiling and managing your personal medical file. Web sites, such as [www.elderissues.com](http://www.elderissues.com) or [http://healthmanager.webmd.com](http://healthmanager.webmd.com), can help you and your loved ones get started. Some of these services may involve an out-of-pocket cost.

Provide your primary care doctor with copies of all tests, prescriptions, or procedures authorized by any other doctors and encourage him or her to communicate with your other doctors as needed.

**The value of a second opinion**

It is perfectly acceptable and reasonable to seek a second opinion whenever you feel the need. Even if your initial diagnosis was made by a neurologist or movement disorder specialist, it is still okay to want and request another opinion—after all, it’s your life!
Communicating effectively with doctors

Although your health is a top priority for your doctor, he or she only sees you during the brief time you are in the office. It is important for you to use your time together to inform your doctor about your PD symptoms, side effects, new prescriptions, and any issues affecting your general health. Come to your appointment with a written list of questions or concerns you want to address. You also may want to bring an effectiveness and side effects diary.

When a doctor asks, “How are you?” it is not a casual greeting. Your answer should never be “Fine,” as if you were making informal small talk. Don’t be afraid to be honest. To do his or her job well, your doctor needs to have an accurate, complete picture about your symptoms and how you’re doing with your treatment. Take this opportunity to discuss problems or improvements that may have arisen since your last visit, such as:

- New symptoms or side effects
- Reduced symptoms or side effects
- Worsening of symptoms or side effects
- Improvement of symptoms or side effects with recent therapy changes
- Things that seem to relieve or reduce symptoms or side effects
- Things that seem to trigger symptoms or side effects—or make them worse
- When new problems started and how they feel

Regardless of what issues you want to discuss during your appointment, use your time with your doctor wisely. Be specific about what you want to talk about, and focus on your PD. If you consistently feel that your doctor does not listen to your concerns or take them seriously, or if you have ongoing difficulty in communicating with him or her, you may want to consider changing doctors. Your ability to communicate with your doctor can influence the quality of your health care.
As a patient, you have a right to keep your health history and medical treatment private. However, you may find it helpful to share your health information with family and friends who are regularly involved in your care.

The Health Insurance Portability and Accountability Act of 1996 (also known as HIPAA) established the HIPAA Privacy Rule, which governs the circumstances under which your health information may be shared with others. If you are present and capable of making your own health care decisions, you must provide permission, or at least not object, to your health care provider sharing your health information with family or friends. The permission need not be in writing, but the office staff may require written documentation for their records. If you are not present or are incapacitated (e.g., unconscious), your health care provider may share your information with your family or a friend if the doctor believes, based on professional judgment, that it is in your best interest.

Ask your physician’s office if they have any policies about sharing your medical information with your family caregivers. If they do, make sure you fully understand those policies. The office may ask you to provide a written note or to sign a form that gives your doctor permission to share your health information with your family caregivers.

At some point, you may decide to have a family caregiver become your legal personal representative. A personal representative can receive your health information and may even make health care decisions for you, if they have your health care power of attorney. Make sure you check your state’s laws on how you can name someone your personal representative.
WATCH FOR THESE SUDDEN HEALTH CHANGES*  

Because PD is a slowly progressing disease, certain sudden changes might indicate another problem. An acute worsening or rapid onset of the following symptoms should be brought to the attention of your nurse or doctor immediately:

- Hallucinations or irrational behavior
- Memory loss or confusion, inability to think clearly
- Behavioral changes such as hyperactivity, tiredness and listlessness, increased or decreased interest in sexuality, intense urges to gamble, or other intense urges
- Gastrointestinal changes such as diarrhea, stomach pain, or worsening of constipation
- Urinary symptoms such as changes in urinary urgency or frequency, discomfort or burning, or change in appearance or odor of urine
- Sudden worsening in motor symptoms such as tremors, dyskinesias, inability to walk, impaired balance, or falling
- Difficulty talking
- Appearance of a new mole or one that changes in size, shape, or color. Because there is a higher risk of developing melanoma (skin cancer) in PD patients, periodic skin exams by a qualified health care provider are advised

*Developed in collaboration with Lawrence Elmer, MD, PhD, director, Parkinson’s Disease and Movement Disorder Program, University of Toledo College of Medicine.
### Planning Your Visit with Your Doctor

Tips from physicians and other health care professionals*

- Whenever possible, bring your family caregiver or another family member or friend to your doctor’s appointments.
- On the other hand, make sure you can arrange a private appointment with your doctor if you need one.
- Before your appointment, write down questions so you won’t forget them. Write down your doctor’s answers during your visit. Recognize that not all questions have answers, especially those beginning with “why.”
- Be clear about what you want to say to the doctor. Use your time efficiently.
- Bring a written list of medications, vitamins, and dietary supplements you are taking, including the medication name, strength, and dosing schedule.
- If you have a lot of things to talk about, request an extended appointment so the doctor can allow enough time to meet with you in an unhurried way.
- Educate yourself about PD and new treatment options as they become available (see page 67, Becoming aware and getting involved).
- Print out any articles about PD that you find interesting to discuss with your doctor at your next appointment.
- Learn the routine at your doctor’s office and/or the hospital so you know how and when to best seek assistance and information.
- Separate your emotions about the challenges of PD from your feelings about the doctor. Remember that you are both on the same team.
- Provide your doctor with an updated copy of your personal medical information.
- Be sure to mention any significant changes in sleep or bowel habits, weight loss, light-headedness or fainting, hallucinations or vivid dreams, dyskinesias (abnormal, involuntary movements), or feelings of confusion or memory loss.
- Make sure you understand all instructions before you leave your appointment.

*Adapted with permission from *Improving Doctor/Caregiver Communications*, National Family Caregivers Association. Available at: [www.thefamilycaregiver.org/caregiving_resources/tips_and_tools.cfm](http://www.thefamilycaregiver.org/caregiving_resources/tips_and_tools.cfm).
Building your team
You are not alone in managing your PD

You have a team of family, friends, and health care professionals who can help lessen the impact of PD on your daily life. You can help them work together for the benefit of your health and well-being. Teams work best when everyone is familiar with the appropriate role of each member and their contribution to the successful execution of your PD game plan. (See the Developing a game plan Chapter on page 18.)

Your role

It is up to you to set the tone for the other members of your care team. You must decide if your approach to PD will be proactive or reactive, passive or passionate. Your care team will follow your lead. It is up to you to communicate with each member of the team so that everyone is working together for the common goal — successful management of your PD. If you feel your spouse or other family member is better equipped to lead your treatment team, it is okay to ask them to advocate for you; just make sure your needs and opinions are always taken into consideration.

You should evaluate the contributions of the members of your care team, letting them know if you need them to contribute more, less, or in a different way. Know when to turn to other members of your team for help.

Your family caregiver

You may be an active, independent person who does not require much care from your family and friends. Nevertheless, there may be a family caregiver or a companion who comes to visit and assist you with your needs — someone with whom you share an emotional bond who helps you make decisions about your approach to PD management, seeks information about PD on your behalf, attends doctors’ appointments with you, or helps you with day-to-day activities. If so, then you have a family caregiver, even though you likely think of them first as your spouse, child, friend, or good neighbor (and they will think of themselves that way, too). Your family caregiver is often a good advocate when you need support in making medical decisions.

Your interaction with your family caregiver will change as you work together to manage your PD. Sometimes this change will be upsetting to one or both of you. Given this, it is important to communicate openly and continue doing the things
you enjoy together. Remember, your PD is challenging and emotional for your family caregiver too. Encourage him or her to make time for personal needs. It is important for both of you that he or she is not overwhelmed by the role of family caregiver. Always remember to express appreciation for his or her support.

**Your doctor**

Your doctor is probably the most influential member of your health care team when it comes to directing your treatment choices. Similarly, a physician assistant (PA) may be very involved in your treatment for PD. PAs are licensed to practice medicine under the supervision of a doctor; they typically conduct physical exams, diagnose and treat illnesses, order and interpret tests, counsel on preventive health care, assist in surgery, and write prescriptions.

Your doctor is best able to help you when you communicate openly and offer as much information about your priorities and needs as possible. (See the Communicating effectively with doctors Section on page 23.)

Your doctor can be a tremendous asset in the management of your PD, but it is important to remember that no one knows everything, not even a doctor you may like and trust. It is okay to probe your doctor’s recommendations and ask for a second opinion when you have questions or concerns about a doctor’s advice. (See The value of a second opinion Section on page 22.)

**Your nurse**

PD specialty centers may employ a nurse educator or a nurse practitioner who is skilled in the area of PD. This person can provide useful information about ways to cope with the physical and emotional challenges of PD as well as available resources. Although your doctor directs much of your treatment, the nurse can be a tremendous resource and assist you along the way. If your doctor has someone like this on staff, speak first with your nurse rather than contacting your doctor initially; the nurse can either assist you or make sure that you speak with your doctor in a timely manner.

**Your physical therapist**

Generally speaking, exercise is an important component to successful PD therapy. However, any mobility, posture, and balance issues that you
experience due to PD may be improved through specific exercises that are developed with the assessment and guidance of a physical therapist. Physical therapists can also help you loosen and strengthen your muscles that may be affected by PD. As a result, you may benefit from improved movement and function.

**Your occupational therapist**

Because PD may affect how well you can perform certain day-to-day activities at home or at work, occupational therapists can help you work on those skills to maximize your independence. Some types of activities that occupational therapists might help with include handwriting, driving, and cooking. In addition, these professionals can help you make changes to your home and work environments to make them safer and easier for you to perform your activities of daily living.

**Your speech therapist**

Working with a speech therapist can help you cope with any changes in speech, voice, and swallowing that you may experience as a result of PD. Early intervention is important in helping you maintain and improve your ability to communicate clearly and swallow. Speech therapists may provide you with exercises to assist in these areas, and they may also provide tips to you and your family for improved communication.

**Your pharmacist**

You may not think of your pharmacist as part of your team of PD professionals. However, pharmacists can do more than dispense medications; they can answer any questions you may have about your medications, and they remain educated about possible interactions that certain drugs may have with others. Pharmacists may also be able to provide information about supplements or over-the-counter medications you may be considering.

**Your mental health professional**

Because many people with PD experience depression, a mental health professional specializing in chronic illness may be helpful. Many mental health professionals can provide education about PD and help you learn new coping skills, such as stress management techniques or other therapies to reduce depression and anxiety.
Talking about your PD

Choosing whether to talk about your PD with family and friends soon after your diagnosis, or later when your symptoms may become apparent, is a deeply personal choice. There are no right or wrong answers to this issue; ultimately, it’s up to you to decide whom to tell about your PD, and when. Eventually, you may find that keeping your diagnosis a secret for an extended period can lead to feelings of anxiety. Others might notice changes in your behavior or how you move before you think they’ll notice, and this might cause some awkwardness in your relationships if you don’t address your condition. Should you decide to share your diagnosis with others, there are ways to communicate with others about your PD that will be helpful and put them in a position to become advocates for you:

• Be honest. Provide as much information as you are comfortable sharing, but feel free to decline to discuss issues that make you uncomfortable.

• Explain that PD is progressive but not fatal. Many people will wonder about the nature of PD, but they may not be comfortable asking.

• Share resources. Tell family members and friends where they can go to learn more about PD.

• Accept assistance. Your family members and friends may feel powerless about your diagnosis. Allowing them to cook a meal for you, do a load of laundry, or offer rides when needed can provide both of you with the satisfaction of being proactive.

• Enlist support. Engage those closest to you in the fight against PD by participating together in fund-raisers or supporting PD advocacy groups. Each of you will benefit from a feeling of taking charge. (See the Advocacy Section in Chapter 11)

Consider seeking a support group to learn how others living with PD have addressed the issue of telling friends and family. A national PD advocacy organization can put you in contact with a local or online support group (see the Selecting a support group Section on page 55), where you can meet others living with PD.
I believe my commitment to high-intensity exercise is mitigating the potential symptoms of Parkinson’s disease. My competition times for sprint triathlons continue to improve. My next endeavor is the Virginia Senior Olympics, then on to the National Senior Olympics. I challenge other people with Parkinson’s to join me!

Cheryl Majeske
Quinton, Virginia
Treatment options
Comprehensive treatment for PD includes not just traditional pharmaceutical medicines, but also a host of other therapeutic approaches, including diet, regular exercise, and a healthy sleep routine.

**Nutrition**

Nutrition is one of the most important things you can focus on to take control of your PD management. In fact, 4 common reasons for hospitalization among people living with PD (bone fracture, dehydration, bowel impaction, and weight loss) can be lessened by proper nutrition.

While most researchers agree there is no specific diet or nutritional supplement to slow the progression of the disease, there are some dietary considerations that may help you avoid diet-related problems and maintain good overall health.

A few healthy habits can ease some food-related challenges of PD. Talk to your doctor about your dietary needs and any food-specific issues related to your medications:

- Drink plenty of water each day, even if you are not thirsty
- Consider eating smaller, more frequent meals each day—or consume healthy snacks between meals. This will compensate for lack of appetite at mealtimes, while ensuring that you receive the right nutrients
- Eat fiber-rich foods daily. Natural laxatives—prunes, vegetables, and foods high in fiber—may prevent or relieve constipation
- Eat something cold and tart, such as lemon sorbet, before a meal to increase saliva production and help with dry mouth
- Maintain a healthy weight to optimize mobility
- Plan meals in advance to ensure that each includes essential vitamins and minerals

Meals high in protein may interfere with the absorption of levodopa. If you find that your response to medication is lessened after a meal high in protein, ask your physician about scheduling a consultation with a registered dietitian.
Incorporating the appropriate amount of calcium into your diet is important to help defend against weakened bones. Muscle mass is lower in those with PD, and this can contribute to lower bone density. Because of an increased risk of falling in PD and potential injury to the bones, regular screenings for osteoporosis are a good idea. If there are concerns about your bone density, your doctor can offer a variety of treatments.

It’s also a good idea to work with a doctor to select a daily multivitamin as “insurance” against poor eating habits. Above all, eating nutritiously and regularly are essential aspects of maintaining good health, so work with your doctor and loved ones to develop a regimen that best fits your personal needs.

You can find more information on recommended daily nutrition allowances and the nutritional content of your favorite foods at www.nutrition.gov.

Exercise

No matter your age or how long you’ve had Parkinson’s, exercise is an extremely important aspect of successful disease management. While exercise will not stop PD, it is crucial in helping to maintain mobility and live well with Parkinson’s. For most people, regular exercise is just as important as taking medications on a routine basis. If you are not exercising regularly, consider starting today! Always consult your doctor before initiating any exercise regimen.

A well-balanced exercise program should include stretching, strengthening, and conditioning activities, and be tailored to your individual needs. Your physician may refer you to a physical therapist or trainer for assistance in developing a program that is best for you. Make sure you are seeing a professional with experience in Parkinson’s disease. (Physical therapy is usually covered by insurance, but you should check with your individual insurance provider.)

Exercise can make you feel more flexible and move more freely. Early research suggests that exercise may even play an important role in maintaining brain function. The benefits of exercise on walking, balance, and range of motion have been demonstrated in clinical trials. Large, exaggerated movements and regular repetition are suggested for maximized exercise benefit.
Some benefits of regular exercise include:

- Improved flexibility
- Increased muscle strength
- Better balance
- Improvements in walking pattern and stability
- Maintained/improved cardiovascular health
- Reduced constipation
- Improved sleep (though exercise right before bed may cause insomnia)
- Increased energy
- A sense of accomplishment
- Improvements in mood
- Reduced feelings of isolation

It may be motivating, fun, and enjoyable to exercise with a buddy or in a group. Others find it helpful to use a video/DVD to help keep their program on track. Maintain realistic expectations of your exercise program, always considering safety first before embarking on a new activity. Take other health concerns (such as arthritis or high blood pressure) into consideration, looking for exercises that improve, not aggravate, other conditions you may have. Your physical therapist can help modify your exercise program if you experience changes in your health or mobility.

**TIPS FOR SUCCESSFUL STRETCHING**

- Stretch until you feel a gentle pull, then hold for 15 to 30 seconds
- Begin with 3 repetitions of each stretch
- Breathe deeply as you stretch—inhale as you stretch; exhale as you relax
- Do not bounce in a stretched position—you run the risk of pulling a muscle
- Do not allow the area being stretched to dangle—find a way to support it
- Don’t push past your limit—overly aggressive stretching, like overexertion, can be detrimental
Regular stretching can help you relieve some of the most common symptoms of PD. Your physical therapist can help you develop stretching techniques to provide some of the following benefits:

- Increased range of motion in your joints
- Improved posture
- Reduced risk of muscle injury
- Improved circulation
- Relief of muscle tension

Some relaxation techniques such as tai chi and yoga combine physical and emotional benefits. Additionally, your local church, mosque, or synagogue may offer programs designed to address your physical and spiritual needs simultaneously.

Whatever exercises you choose, they should be done regularly and in moderation. The most important thing is to find something you enjoy and stick with it. Start out slowly and increase your activity within your comfort zone.

The American Council on Exercise (www.acefitness.org) can provide more information on the importance of physical activity in maintaining good health. You may also seek out exercise programs addressing the specific needs of people living with PD, such as the Parkinson’s Disease Foundation’s Motivating Moves exercise video (www.pdf.org), or through PD advocacy organizations (see pages 75-76).

**Healthy sleep**

Achieving restful sleep is important to your overall health and keeps both body and mind functioning properly. People living with PD often experience sleep difficulties, including vivid or overactive dreams, sleeplessness, restless legs, and daytime drowsiness. There are a number of practices you can adopt to increase your ability to get a good night’s sleep regularly:

- Avoid alcohol and caffeine or other stimulants, especially in the evenings
• Avoid oversleeping—sleep just long enough to feel refreshed
• Avoid watching TV, reading, or eating in bed
• Create the most comfortable, peaceful environment possible at bedtime
• Exercise regularly
• Limit bright light exposure in your bedroom at night
• Go to bed and get up at the same time each day; follow a regular relaxing bedtime routine
• Try wearing socks
• Minimize fluid intake in the evening before bedtime

Some people living with PD experience restless legs syndrome (RLS) while trying to fall asleep or when inactive. RLS is sometimes described as a pulling, tingling, or aching feeling in the legs. The discomfort usually improves with movement of the legs (hence the name “restless legs”) or walking. Although the cause is unknown, some medications can help to alleviate RLS, so speak with your doctor if you experience these sensations.

Your PD medications may interfere with your sleep patterns and cause insomnia or sleepiness. It is important to achieve sufficient rest to feel your best and ease other challenges of living with PD. If, after trying the tips above, your sleep difficulties do not improve, talk to your doctor about medications that might help relieve your severe sleep complications. He or she may refer you to a sleep specialist who can identify strategies to improve your sleep.

Additionally, there are many over-the-counter sleep aids. Some have side effects or may interact adversely with your PD medication, so you should always discuss these medications with your pharmacist as well as your physician before trying them. For more information on the importance of sleep for optimal health, visit the National Sleep Foundation at www.sleepfoundation.org.
Medications for PD

Thanks to research conducted in recent decades, many treatments are available to help manage PD. You and your medical team will select the best treatment approach for you based on your symptoms and needs.

Although there is not yet a cure for PD, medications can help you manage your symptoms, both in the short and long term. The goal of treatment is to maximize the management of symptoms while minimizing troublesome side effects. Since all PD treatments have potential side effects, you should work with your doctor to determine which medication is right for you.

Many PD treatments can be used alone (referred to as monotherapy) or in combination with one another (referred to as adjunct therapy).

Most available medications for PD treat dopamine deficiency by either 1) helping to replace dopamine, 2) preventing its breakdown, 3) mimicking the effects of dopamine, or 4) some combination of these benefits. Finding the right medication or combination of medications depends on your individual needs and how sensitive you are to various treatments. Here is a brief overview of some of the medications that fall into each of these 4 categories:

**Medication that helps to replace dopamine: levodopa**

It has been more than 30 years since levodopa first provided symptom improvement in people with even the most severe symptoms of PD, and it remains one of the most effective treatments. It’s called a precursor because it can be taken orally to enter the brain, and then the brain can convert it into dopamine. This helps to replace the brain’s diminished supply of dopamine. Levodopa is used because dopamine, if given in oral form, does not enter the brain.

Levodopa was found to be very successful at reducing tremors, slowness, and other symptoms during early stages of PD. However, as the disease advances, levodopa’s symptomatic benefit becomes less predictable. Long-term use of levodopa also increases the risk of complications, such as dyskinesias (involuntary movements) and/or motor fluctuations (the “on-off” effect — “on” is when a person’s treatment is working and relieving the symptoms of PD, and “off” is when the treatment is not working or providing relief from symptoms.

Please see important safety information on pages 44-45.
of PD). This is why it has become common practice to look at other medications to use as initial therapies for early PD or in conjunction with levodopa at all stages of Parkinson’s. In some cases, the choice may be made to wait to use levodopa in order to delay the risk of complications in later stages of PD—especially in younger patients, who are more likely to have complications from long-term levodopa therapy.

Examples: SINEMET®, SINEMET CR® (carbidopa/levodopa, carbidopa/levodopa ER) and PARCOPA® (carbidopa/levodopa orally disintegrating tablets).

Medications that help prevent the breakdown of levodopa or dopamine: enzyme inhibitors

In general, enzymes are like miniature factories, promoting the conversion of one substance into another, while enzyme inhibitors slow or stop this process, effectively blocking the effect of the enzyme. PD treatments that fall under this class of medications target specific enzymes that manage the levels of dopamine in the body. These medicines are enzyme inhibitors that may 1) block the enzymes that break down levodopa (a chemical precursor of dopamine), or 2) block the enzymes that destroy dopamine once it is in the brain (whether the dopamine is formed from the brain itself or from levodopa given for the treatment of PD).

SINEMET® is an example of a medication that contains levodopa plus the chemical carbidopa, which helps prevent a certain enzyme from breaking down levodopa before it reaches the brain. By blocking the enzyme that causes this breakdown, more levodopa can cross into the brain and be converted into dopamine. Carbidopa can also reduce certain side effects of levodopa, including nausea, vomiting, and blood pressure problems. Carbidopa is universally given simultaneously with each dose of levodopa in a single pill or may be given as a separate pill for additional benefit. Carbidopa alone is generally not associated with side effects, but it helps prevent side effects of levodopa.

Although the combination of carbidopa with levodopa helps to make more levodopa available to the brain, some levodopa is destroyed in the intestines and liver by another enzyme called catechol-O-methyltransferase (COMT). By blocking the action of this enzyme, COMT inhibitors allow more levodopa to be transported into the brain to be converted to dopamine. COMT inhibitors
Treatment options

are only prescribed together with carbidopa/levodopa therapy and have been shown to reduce “off” time in patients taking levodopa. COMT inhibitors may be prescribed several times per day or with each dose of carbidopa/levodopa. In one medication, the COMT inhibitor entacapone is combined with carbidopa/levodopa in one pill. In some cases, the dosage of levodopa can even be reduced when entacapone is added which, in turn, may help reduce side effects from excessive amounts of levodopa. However, side effects of this class of drugs may include dyskinesia, nausea, diarrhea, abdominal pain, and urine discoloration.

MAO-B (monoamine oxidase type B) inhibitors are another category of enzyme inhibitors used to treat PD. This type of inhibitor blocks the actions of the MAO type B enzyme, which is responsible for the majority of the breakdown of dopamine inside the brain, and therefore, treatment with MAO-B inhibitors usually increases dopamine levels in the brain. When used as initial therapy in treating early symptoms of PD, MAO-B inhibitors may be used alone to help control motor symptoms while delaying the need for levodopa or other therapies. When prescribed along with carbidopa/levodopa therapies, MAO-B inhibitors have also been shown to reduce “off” time. MAO-B inhibitors may be given once or twice daily in different dosage forms. Some side effects of MAO-B inhibitors include muscle twitching and cramping, depression, headaches, and indigestion when used alone, as initial therapy. When these medicines are used with levodopa, additional side effects may include dyskinesia, nausea, dizziness, and low blood pressure when standing.

Of all the treatments used for PD — whether for early management of PD ([AZILECT® [rasagiline tablets]]) or for advanced symptoms of PD (all other enzyme inhibitors listed below) — the enzyme inhibitors such as rasagiline and entacapone are considered to have lower dopaminergic side effects.

Examples: AZILECT® (rasagiline tablets) and ELDEPRYL® (selegiline), MAO-B inhibitors; COMTAN® (entacapone) and TASMAR® (tolcapone), COMT inhibitors; LODOSYN® (carbidopa), a dopa decarboxylase inhibitor; and STALEVO® (carbidopa/levodopa/entacapone).

AZILECT® is indicated for the treatment of the signs and symptoms of Parkinson’s disease (PD) both as initial therapy alone and to be added to levodopa later in the disease. AZILECT® is a once-daily treatment for people with Parkinson’s disease.
Medications that mimic the effects of dopamine: dopamine agonists

Dopamine agonists (DAs) work by acting like “keys” to dopamine receptor “locks” in the brain, thus mimicking the effects of dopamine. DAs may be used alone in patients newly diagnosed with PD, but they may also be used in combination with levodopa and/or other treatments. Used in combination with carbidopa/levodopa compounds, they may reduce “off” time. DAs can be effective during early stages of PD to help control tremors, stiffness and slowness of movements, as well as night-time leg cramping. New extended-release formulations add the convenience of once-daily dosing. All of the DAs are taken as tablets, except for APOKYN®, which is an injection that can be used as a rescue medication to manage “off” periods.

DAs have potential side effects that include nausea, dizziness, sleepiness, dyskinesia, peripheral edema (swelling of the hands and/or feet), along with confusion or hallucinations when used alone. Behavioral effects of these medications have also been recognized in recent years, and some people may experience compulsive eating, gambling, increased sexual urges, or other reward-seeking behaviors.

Examples: APOKYN® (apomorphine), MIRAPEX® and MIRAPEX ER® (pramipexole), NEUPRO® (rotigotine), PARLODEL® (bromocriptine), and REQUIP® and REQUIP XL™ (ropinirole).

Medications with other actions

SYMMENTREL® (amantadine) may provide relief for symptoms of PD. It provides mild benefits for symptoms of tremor, stiffness, and slowing activity or movement in early PD, but may also be prescribed in advanced PD to help reduce dyskinesias. It has potential side effects of dry mouth, constipation, and/or hallucinations, as well as skin discoloration. COGENTIN® (benztropine) and ARTANE® (trihexyphenidyl) act by blocking acetylcholine and may be useful for the treatment of tremor. These medications have frequent side effects of dry mouth, constipation, confusion, and memory loss. The use of SYMMETREL®, COGENTIN®, and ARTANE® in older patients may be associated with mental side effects, including the confusion and memory loss as mentioned above. Their use in people above age 65 (and in some cases, even younger) should be monitored very carefully.
Examples: SYMMETREL® (amantadine), COGENTIN® (benztropine), ARTANE® (trihexyphenidyl), and EXELON® (rivastigmine).

You should discuss with your doctor the possibility of using other medications for nonmotor problems that may be related to PD, such as memory loss, depression and anxiety, sexual dysfunction, problems with sleep, hallucinations, and bladder and bowel problems. Often there are treatments available that can be helpful. One example is EXELON® (rivastigmine), which can help symptoms of PD (for example, dementia) if this occurs. First and foremost, if you’re experiencing problems including any side effects (especially confusion and/or hallucinations/delusions), you should discuss these with your health care provider immediately, as these symptoms may be an indication that a particular medication or combination of medications is reacting poorly inside your body and brain.

The indications and side effects listed in the above drug classes are not necessarily those of a specific drug, but rather of the broader class of drugs to which it belongs. For information on indications and the potential side effects of a specific drug, read the information found in the drug package provided by your pharmacy or ask your doctor or pharmacist. Remember also that indications and side effects during the treatment of PD are individualized, meaning that each person should review his/her therapy’s effectiveness and/or side effects with their clinician.

Important safety information regarding AZILECT® (rasagiline tablets)

Do not take AZILECT if you are taking meperidine as it could result in a serious reaction such as coma or death. Also, do not take AZILECT with tramadol, methadone, propoxyphene, dextromethorphan, St. John’s wort, or cyclobenzaprine. You also should not take AZILECT with other monoamine oxidase inhibitors (MAOIs).

Inform your physician if you are taking, or planning to take, any prescription or over-the-counter drugs, especially antidepressants and ciprofloxacin. If you have moderate to severe liver disease, you should not take AZILECT. You should not exceed a dose of 1 mg per day of AZILECT in order to prevent
a possibly dangerous increase in blood pressure. All PD patients should be monitored for melanoma (skin cancer) on a regular basis.

Side effects seen with AZILECT alone are flu syndrome, joint pain, depression, and indigestion; and when taken with levodopa are uncontrolled movements (dyskinesias), accidental injury, weight loss, low blood pressure when standing, vomiting, anorexia, joint pain, abdominal pain, nausea, constipation, dry mouth, rash, abnormal dreams, and fall.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

**Tips for managing your medication**

Successfully managing the treatment of your PD symptoms may require the use of more than one medication. As your PD progresses, the number of medications prescribed and frequency of their dosing can become complicated. Here are a few guidelines to help your medications work best for you.

- Ask for clear written instructions from your doctor, nurse, or pharmacist. Familiarize yourself with your prescriptions. You should know the side effects, dosage information, and designated restrictions. Make sure your doctor and/or pharmacist provides this information to you.

- Write on each prescription bottle the name of the illness it treats. This will make you aware if you are taking several medications for the same condition — something you should discuss with your doctor.

- Follow instructions exactly as they are given. The effectiveness of some medications is affected by other factors, including diet and the timing of your food intake relative to when you take your medications. Foods high in protein (meat, fish, cheese, milk and milk products, nuts, beans, etc), for example, may interfere with the absorption of some medications such as levodopa. Even instructions that seem unimportant to you may alter the effectiveness and safety of a prescription.

- Develop a system for consistently taking your medications. You may want to use a daily or weekly pill organizer, a timer, the alarm on your cell phone, or an alarm clock to maintain your medication schedule.
• Keep a list of your daily medications taped to the refrigerator or displayed in another prominent place, and keep another copy in your wallet for easy reference at home or away. Consult your doctor before taking any additional medication, including antibiotics, pain relievers, sleep aids, allergy and cold medications, and dietary supplements, regardless of whether they require a prescription or are sold over the counter.

• Purchase all of your prescriptions from the same pharmacy, so they have a comprehensive record of your current treatment regimen and can help you watch for potential drug interactions.

• Share the responsibility of managing your medications with your family caregiver. Neither of you should be solely responsible for managing all of these details.

Managing medications during hospital stays

It is easy for medication schedules to be interrupted during hospital stays when attention for an immediate medical concern, such as a surgical procedure, can shift the focus away from your PD. Your PD symptoms could worsen during such times due to the physical stress of your medical illness or surgery, changes in sleep patterns or diet, lack of activity, dehydration, changes in medication timing or dosage, or even having to stay off medications for a short time.

If you are hospitalized, remind doctors and nurses of your PD diagnosis as well as any other medical conditions you have. Inform them of all of your current medications and the timing of each dose as well. Insist that this information be added to your hospital chart. Make sure a family member or friend has an updated copy of your personal medical information. Ask him or her to provide it to your admitting nurse and the appropriate doctor, and make sure this information is included in your hospital chart. You may also want to carry a copy of your personal medical information in your wallet or purse. If you are staying in the hospital for a significant period of time, requesting a consultation from a PD specialist or neurologist could be helpful: while major changes in your PD medications may not be advisable, they may be able to help keep your symptoms better controlled during the hospital stay.

Please be aware there are now dosage forms of PD medications that are available besides pills in case your doctor withholds you from taking anything by mouth.
Options for surgical treatments

Several types of brain surgery have emerged as treatment options if currently available medication is not effective or if your symptoms have progressed to the point that prescription medications no longer offer benefit. For more information about surgical options, talk to your doctor. You may also consult the Web sites listed below or those of national PD advocacy organizations (see pages 75-76).


http://www.wemove.org/par/par_sur.html


Deep brain stimulation

In deep brain stimulation (DBS), neurosurgeons implant an electrode into an area of the brain that affects movement. The electrode delivers a continuous high-frequency electrical stimulation, helping control the movement centers in the brain. The implants can be placed on one side or on both sides of the brain as needed to control symptoms. DBS frequently leads to a dramatic improvement in PD symptoms and may allow for a reduced dose of levodopa, which may reduce and/or eliminate levodopa-related side effects and complications, such as dyskinesia.

People with PD should always consult with a movement disorder specialist with DBS experience before considering this option. You can find such specialists by calling one of the national PD advocacy organizations (see pages 75-76). In addition, some world-class centers have emerged throughout our country that have superior results in performing this surgery. It’s a major decision, and you owe it to yourself to “shop around.” There can be very serious complications of brain surgery; for example, memory problems may be made worse. There is also a very small risk of stroke, seizures, hemorrhage, and/or infection, especially around the time of the surgery. As with any type of surgery (especially brain surgery), make sure an expert neurological and neurosurgical consultation has been completed to confirm that this is the right option for you before proceeding.
Looking to the future

Research by universities and pharmaceutical companies has resulted in tremendous advancements in the treatment of Parkinson’s disease, especially with regard to effectiveness and convenience. The number of medication treatment options has grown as new methods of increasing dopamine and balancing other brain chemicals are developed. Different administration methods are available and continue to be investigated. The goal is to provide an even, steady level of dopamine to the brain for the best motor functioning possible.

Basic science research also gives us much to look forward to in the future. Although PD is usually not inherited in families, significant discoveries about genetic (inherited) abnormalities in PD will hopefully lead to greater understanding of the possible reasons people develop PD. There are a few genes (parts of our DNA) now known to be implicated in PD. The more we learn about the way these abnormalities promote brain cell death, the better we may understand how to prevent this damage and develop treatments that prevent cell loss and disease progression.

Current clinical research using new medications is focused on 1) slowing down disease progression, 2) discovering better treatment of motor symptoms such as freezing and balance, symptoms that current medications do not adequately help, and 3) finding better treatments of nonmotor symptoms, such as dementia and others. Scientists are now investigating ways to correct the cause of nerve cell death (including dopamine cell death) and/or improve dopamine production and release. Recent research indicates that many nerve cells throughout the body are damaged by PD, not just the dopamine nerve cells. For this reason, the initial thought of using stem cells to correct a “dopamine-only” disease is not clearly the final answer to correct this disease. However, while we may not achieve a cure for PD using stem cells, there is hope that new stem cell technologies, including adult stem cell technology, will accelerate our understanding of PD and development of new treatments.

Participating in clinical trials

Every PD treatment approved by the US Food and Drug Administration (FDA) must go through extensive testing of its safety and efficacy before
doctors can prescribe these treatments to patients. This process requires clinical research and the participation of many people diagnosed with PD. Participation in a clinical trial may offer you several benefits, including:

- Taking a more active role in the management of your PD
- Gaining access to experimental treatments before they are FDA approved
- Receiving quality medical care free of charge for the duration of the trial
- Helping to advance the knowledge and treatment of PD by participating in medical research

If you participate in a clinical trial, the procedures involved, including any possible risks and benefits, will be explained to you. You will be asked to sign a consent form before the trial begins. You may end your participation at any time and for any reason, and you can work with your doctor to identify additional treatment options.

TO LEARN ABOUT OPPORTUNITIES TO PARTICIPATE IN CLINICAL TRIALS, VISIT THE FOLLOWING WEB SITES

www.pdtrials.org
A comprehensive listing of clinical trials in PD maintained by the Parkinson’s Disease Foundation

www.centerwatch.com/patient/studies/cat117.html
Listings of clinical trials in PD by state

http://clinicaltrials.gov
General information from the National Institutes of Health (NIH) about clinical trials

www.ninds.nih.gov/parkinsonsweb
Information from the National Institute of Neurological Disorders and Strokes (NINDS)

www.parkinson-study-group.org
Information about clinical trials being conducted in the United States by the Parkinson Study Group

Web sites of PD advocacy organizations (see pages 75-76 for listings)
Alternative therapies: facts, fallacies, and myths
Some people benefit from alternative treatments that may complement your established PD therapies. It is essential that you discuss any of the following treatments with your doctor, especially if they involve over-the-counter or nonprescription medications, dietary supplements, or other treatments.

The National Center for Complementary and Alternative Medicine offers comprehensive information about these types of treatments at http://nccam.nih.gov, and national PD advocacy organizations offer additional information about alternative and complementary treatments in PD. (See page 79 for listings.)

Remember: while some alternative therapies can be helpful, others can be ineffective, costly, and even dangerous. If you are interested in a particular alternative treatment, make sure you protect yourself. Do not accept any claims for any treatment without fully investigating them first. Some warning signs that a treatment might not be legitimate include:

- If the treatments or their providers are promoted through telemarketers, direct mailings, infomercials, ads that look like real news articles, or ads in the back of magazines
- If the treatment claims to be a cure for PD, or makes other outrageous claims
- If the treatment is only available through 1 manufacturer
- If any treatment ingredients are secret or unlisted
- If testimonials for the treatment are paid endorsements (meaning that the person giving the testimonial is getting paid to make those claims about the treatment)

As you research alternative treatments, contact the Better Business Bureau to learn more about the treatment provider. Do not undergo or accept treatment with any providers who do not want to work with your doctor. Find out what the treatment will cost; most alternative treatments for PD are not covered by insurance.

Finally, make sure you consult with your doctor and pharmacist about any alternative treatments you are considering. They can help you understand any
possible side effects or interactions that might result between the therapy you’re considering and your existing treatment regimen. Your doctor may also be able to provide information on what other patients may have experienced when using a particular alternative treatment.

**Acupuncture**

Acupuncture is an ancient Chinese holistic technique involving placement of tiny needles into certain points on the body to restore balance to the body’s flow of energy. There is limited evidence that acupuncture may provide benefits in PD. If you are considering acupuncture, ask your physician for a recommendation and only use an acupuncture therapist who is trained and licensed by an organization such as the National Certification Commission for Acupuncture and Oriental Medicine or the American Academy of Medical Acupuncture. For more information about acupuncture, consult [www.medicalacupuncture.org](http://www.medicalacupuncture.org).

**Dietary supplements and herbal medications**

Some herbal extracts claim to be beneficial for certain symptoms of PD or help alleviate side effects of PD medications. Because these supplements are not as strictly regulated by the FDA as medications are, there is often no clinical proof of their efficacy, and there may be significant variation in their potency and purity. These agents can interact with your medical treatments, so always discuss the addition of a dietary supplement or herbal medication with your doctor or pharmacist. Information about the potency and purity of many health supplements can be found at [www.consumerlab.com](http://www.consumerlab.com).

**Massage therapy**

Massage, when properly administered by a licensed professional, may provide relief from rigidity and other motor symptoms you may experience, and the relaxation effects of massage therapy may provide benefits. You can learn more about massage therapy at [www.amtamassage.org/index.html](http://www.amtamassage.org/index.html).
**QUESTIONS ABOUT ALTERNATIVE THERAPIES**

When considering an alternative treatment for your PD, be sure to ask yourself the following questions:

- What is the alternative treatment?
- How does it work?
- What is the proof that it works?
- Why does it work?
- What are the risks, if any?
- Are there any side effects?
- How much does it cost?

*Adapted from WebMD.

**Mind-body connection**

Therapies that focus on the mind-body connection are designed to address the interaction between the brain, mind, body, and behavior, which consequently affect overall health. Mind-body interventions have demonstrated positive effects on psychological function and quality of life, and may be especially valuable for people who have a chronic illness.

Activities that enhance the mind-body connection include relaxation and spiritual techniques, such as

- Tai chi, an ancient form of Chinese exercise that teaches gentle body movements to improve flexibility and balance
- Visual imagery and controlled breathing techniques, such as yoga
- Music therapy using selections that appeal to you
- Spiritual health through personal introspection, prayer, or other forms of personal reflection
Emotional well-being
Staying engaged with your life

Your emotional well-being is important

Living with PD brings a range of emotions, including apathy—a feeling of indifference or not caring much about anything. Tending to your emotional health is as important as tending to your physical health. Support groups are a great way to cope with some of the emotional challenges of living with PD. Some people may prefer choosing a friend or two to talk to regularly.

Regardless of how you express yourself emotionally, it’s important to stay connected with other people in some manner for your emotional well-being.

Friends and family

It’s easy for people with PD—especially in the early stages of the disease—to feel embarrassed about their symptoms. As a result, it might feel tempting to withdraw from family, friends, and other social contacts, but this may lead to feeling isolated and depressed. Keeping in active touch with others is an important factor in your mental and emotional health; it can help you feel in control over your life again. Don’t be afraid to share your thoughts, feelings, hopes, and fears with your loved ones and friends. You may find that your relationships with these special people in your life become deeper. Try taking time to participate in social events at a place of worship, attend concerts and classes, entertain friends at home, and volunteer; you’ll find this time spent interacting with others well worthwhile.

Selecting a support group

You have many choices when it comes to selecting a support group. You can participate in a support group in your community or in a virtual (Web-based) support group. The title “support group” may conjure up an image of a group of people sitting in a circle and talking about their feelings. While this type of emotional support serves an important function, there are other types of groups as well. Some groups focus on educating their members about PD and advances in treatments or the search for a cure; others offer practical advice for managing PD, allowing members to share what has worked best for them and to learn from one another.
Many PD advocacy groups offer listings of community or Internet support groups (see pages 75-76 for listings). Your doctor or nurse may also be able to recommend a group in your area. It is important that you find a support group that is a good match for your personality and current needs.

Prior to attending, you should contact the leader of the support group to inquire about the group’s focus and format. Feel free to attend several support groups until you find one that suits your needs. If you are unable to find an existing group that meets your needs, consider starting your own. You can work with a national or local PD advocacy group, nurse, or social worker to lay the foundation for a new support group. The National Family Caregivers Association has a guide to help you choose a support group at www.thefamilycaregiver.org/caregiving_resources, in the Tips and Tools section.

Dealing with depression

As is the case with any patient who has a chronic condition, you may be vulnerable to having feelings of apathy or depression. In fact, the feelings associated with PD are often complicated by depression: as many as half of those living with PD may experience clinical depression at some point. Addressing depression is important to your overall well-being. Occasional feelings of sadness or discouragement are normal, but you should watch for signs that you may be experiencing clinical depression and discuss them with your doctor. Depression that occurs in PD can be treated with antidepressants and other approaches, such as physical activity and counseling.

Family caregivers may also experience depression or need to find help. Your doctor can help you decide whether an antidepressant is right for you and refer you to a reputable therapist in your area. Social workers and faith-based counselors may also be helpful in dealing with the emotional ups and downs of PD.
**SYMPTOMS OF DEPRESSION**

- Persistent sad, anxious, or “empty” mood
- Feelings of hopelessness or pessimism
- Feelings of guilt, worthlessness, or helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy or feeling overwhelmed, fatigued, or like “your get up and go, got up and left”
- Difficulty concentrating, remembering, or making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight changes
- Thoughts of death or suicide, or suicide attempts
- Restlessness or irritability
- If 5 or more of these symptoms are present every day for at least 2 weeks and interfere with routine daily activities such as work, self-care, child care, or social life, seek an evaluation from your doctor for depression

*Adapted with permission from *Symptoms of Depression*, National Institute of Mental Health NIH Publication No. 02-500.*
Balancing your work and personal life

Managing activities of daily living

Although you have been diagnosed with PD, you may continue most of your everyday activities. In the later stages of PD there is more difficulty performing activities of daily living, but even then, small modifications to your daily routine can ease many of those challenges.

If you start to have difficulty with your daily tasks, consider consulting some of the publications offered by PD advocacy organizations, which contain helpful tips for dealing with tasks of daily living, or any of a number of helpful books on the topic. You should also discuss these issues with your doctor or nurse for 2 reasons: 1) he or she can refer you to helpful resources; and 2) increased difficulty with activities of daily living may indicate a need to adjust your medication dosing or otherwise modify your treatment regimen.

You may also want to consider getting your doctor’s referral to an occupational therapist. These specialized therapists can teach you techniques and give advice on equipment that can help you better manage your activities of daily living. Occupational therapists can also advise you on changes to your home environment that will help you maintain your independence, while making your home more safe and comfortable for you.

Work

Most people are able to continue their lifestyle, including working, for some time after their PD diagnosis. As time goes by, your physical symptoms may start to cause challenges with some of your work activities. Again, consider talking to an occupational therapist about your specific challenges. Occupational therapists can provide skilled treatment and suggestions that will help improve your work environment for your special needs. In the meantime, there are other steps you can take to minimize the impact of those challenges:

- Know which times of day your medications are most effective, and plan to work on your most-challenging assignments during these windows of “optimum performance”
• Discuss alternative work arrangements with your employer, such as consulting or reduced hours

• Address workplace accommodations that may allow you to remain on the job

• Know your rights under the Americans with Disabilities Act. Learn more at www.eeoc.gov/laws/types/disability.cfm. You may also take advantage of the Family and Medical Leave Act (FMLA) if your appointments are jeopardizing your or your family caregiver’s career. Go to www.nationalpartnership.org for more information

Choosing when or if you should discuss your PD with an employer or coworker is a very personal decision. You may find that sharing your diagnosis opens the door to additional sources of support, or you may choose to manage your disease privately. Because there may be consequences to your employment, you will need to think this through clearly.

Keep in mind that PD may affect your job performance, especially if your work requires manual dexterity or mental focus: for example, an airline pilot or surgeon would probably have to inform their employer about their condition sooner than a salesperson might. Also, despite federal laws that prohibit firing people with disabilities, your employer may reassign you to another job or pressure you into early retirement. On the other hand, your boss may make accommodations to help you keep doing your job or allow you to work from home.

Regardless of how you decide to approach this issue, you may want to discuss this decision first with others living with PD who can offer the benefit of their own personal experiences.

**Hobbies and interests**

Hobbies are an important part of life, and they should be a priority when it comes to managing your PD. Having things you enjoy and look forward to doing are essential to your emotional well-being. Make time for your hobbies and interests, and talk to your nurse or doctor if PD symptoms or medication side effects interfere with your ability to do them.
Though some skills may become more difficult as PD progresses, there are things you can do to continue the activities you enjoy:

- Bring a buddy—invite a friend or family member to participate in your hobby with you and allow her or him to help as needed. For example, if you enjoy fishing but find baiting your hook difficult, you can ask a buddy to assist with that task, allowing you to continue enjoying the sport.

- Look for adaptive equipment—if not readily available for your hobby, consider enlisting a specialist to create an adaptive tool for you. Organizations such as AbleData (www.abledata.com), the Adaptive Sports Association, (www.asadurango.org), or the National Sports Center for the Disabled, (www.nscd.org) may get you pointed in the right direction.

- Expand your interests—try new activities that may be less physically challenging, or find new ways to participate. If you can’t participate in the traditional sense, perhaps you can teach, officiate, or coordinate events. You also may want to consider expressing yourself in some type of creative outlet, such as writing or painting.

### Planning for the future

Managing your well-being in your life with PD also means looking toward your future as a PD patient. At some point you may become unable to make important decisions about your treatment and care. You can provide your family caregivers with some relief from stress by addressing certain issues today about your care in the years ahead. Creating advanced directives, such as a living will or designating a durable power of attorney, can help ensure that your wishes about your care will be followed. It is never too early to begin creating these directives, and you should not postpone this process until you are facing any serious health issues. When you're taking steps to address your future care, make sure you check your state’s laws about their requirements for any related documents.
Paying for your care
Health care insurance coverage, including government-sponsored programs such as Medicare and Medicaid, is complicated and, at times, intimidating. Undoubtedly, the complexities of coverage will evolve as new mandates and programs based on the recent Patient Protection and Affordable Care Act are introduced.

Based on the continuing shifts in health care policy and insurance plans, it is important that you stay informed about your health care coverage and that you learn how to address questions that may arise.

**Handling the gaps in health care coverage**

Much health insurance today is provided through managed care organizations, such as health maintenance organizations (HMOs) or preferred provider organizations (PPOs). Medicare and Medicaid also offer federal health insurance coverage options for individuals age 65 and older, certain persons under age 65 with disabilities, and individuals who are uninsured and have limited income.

While HMOs, Medicare, and Medicaid may provide coverage for most of your doctor visits, hospitalizations, and medications, they may also impose restrictions on your access to care. It is vitally important you understand those restrictions, as they will affect your ability to meet your medical needs and expenses.

However, a range of organizations, agencies, and individuals are available to assist you in obtaining the extra help you may need for adequate, affordable medical care:

- Allsup ([www.allsup.com](http://www.allsup.com)) provides assistance with claims made for Social Security Disability Insurance (SSDI) and Medicare benefits, only charging a fee if a claim is approved

- Claims Assistance Professionals may be found through [www.claims.org](http://www.claims.org); these individuals can be hired to help organize health insurance paperwork, review medical bills and determine proper payment, track claims, challenge denials of claims, and negotiate providers’ fees, among other services
• The Patient Advocate Foundation (www.patientadvocate.org) is a national nonprofit organization that helps patients with specific issues related to access to care; their case management services and educational materials are free of charge

• Patientassistance.com and RxAssist.org provide searchable online databases of prescription assistance programs, which may help patients access the medications they need for free or at a low cost. Needymeds.com offers a similar database, as well as information on disease-based assistance programs designed to help patients handle costs of specific diseases and conditions

• The Medicare Rights Center (www.medicarerights.org) is a nonprofit group that works to ensure access to affordable health care for older adults and people with disabilities through counseling and advocacy, educational programs, and public policy initiatives. The Center’s Medicare Interactive Counselor (www.medicareinteractive.org) provides up-to-date answers on common questions regarding Medicare coverage, as well as links to relevant state and national resources

• The Helen M. Lynch Direct Aid Fund, established by the Parkinson’s Disease Foundation and the Melvin Weinstein Parkinson’s Foundation (www.mwpf.org/index.htm), was created in 2008 to help eligible patients cover the costs of PD-related care or medical equipment

Medicare patients with limited income and resources also may benefit from assistance through the Extra Help/Low Income Subsidy program, which helps eligible patients with their Medicare prescription drug plan costs. To qualify, patients must meet the program requirements for annual income and financial resources, such as bank accounts, stocks, and bonds.

In 2010, the eligibility requirements for this program were changed. For example, life insurance policies are no longer counted as a resource, and any help received from someone else on food, shelter, and household bill payments is no longer considered income. To learn more about the Extra Help/Low Income Subsidy program, visit the program Web site at www.socialsecurity.gov/prescriptionhelp/index.htm and click on the first link, “Information on the Extra Help program.”
Help for those who are uninsured or unable to pay for medications

Many pharmaceutical companies have programs that provide prescription medications to uninsured patients or those with a limited income. Your doctor or pharmacist can help you to enroll in one of these programs.

TIPS FOR WORKING WITHIN YOUR INSURANCE PLAN

- Know the details of your plan and watch for updates about coverage. Understand what is covered, how to submit claims for reimbursement, and how you can dispute a claim decision.

- Learn who can answer your questions. If you are insured through an employer, a human resources person or administrator may be able to answer some of your questions. Keep the phone number for your insurance provider’s customer service department handy.

- If you find that filing claims or communicating with insurers is overwhelming, ask if your doctor’s office has resources to help.

- Keep comprehensive records (see the Managing treatment with multiple doctors section on page 22). Record the date and nature of doctors’ appointments and procedures. Document all communication with your insurance company—record the dates of calls, the person(s) with whom you speak, and the conversation outcomes. Don’t be afraid to dispute a claim. If you feel a billing or ruling regarding a claim is incorrect, pursue it.

- Be patient. It can take weeks, or even months, to settle a claim. It is important that you see your claims through to resolution so you do not pay more than you should.

- You may also appeal Medicare Part D coverage denials or file a complaint within 60 days. For more information, visit www.medicare.gov.
Getting involved
Even if you manage your PD proactively, you may occasionally feel at the mercy of this disease. But there are many things you can do to fight back. It is important to expand your focus beyond your personal health from time to time. Advocacy and activism can have a positive effect, allowing you to contribute to the entire PD community.

**Becoming aware and getting involved**

The first step in fighting back is to become your own advocate. Arm yourself with as much information as you can about PD. In addition to becoming familiar with your own symptoms, treatments, and side effects, consider staying up-to-date on the latest news about PD. Most national PD advocacy groups offer news updates on their Web sites (see pages 75-76), and services such as [http://news.google.com](http://news.google.com) can deliver news about PD directly to your e-mail inbox. Some pharmaceutical companies also offer free newsletters to keep you up-to-date on advances in PD. One such newsletter is available by registering at [www.parkinsonshealth.com](http://www.parkinsonshealth.com).

If you're interested in hearing the very latest advances in our understanding of PD and treatment practices, you might want to consider attending a scientific conference about PD. The World Parkinson Congress ([www.worldpdcongress.org](http://www.worldpdcongress.org)) is one example of a scientific meeting that encourages attendance by all people who are affected by PD—from researchers and clinicians to patients and family caregivers. Attending these kinds of meetings may help you feel more knowledgeable about PD—and more connected to the PD community. If you're not able to attend a conference in person, you may be able to watch certain presentations and lectures through an Internet webcast, which may be broadcast live or recorded.

Awareness of the latest advances and new PD treatments may be beneficial to your personal disease management. When you find information you believe is relevant to your treatment, take it to your doctor. He or she can explain why this information may or may not impact the way you approach your PD.
Fund-raising

Fund-raising for research, patient support efforts, or PD advocacy organizations is something you can do independently or together with friends, family, neighbors, or your community at large. People who care about you will care about PD. Your personal experience can be a catalyst for action in those around you.

Find a local or national PD advocacy group you like and trust, and seek opportunities to participate in their fund-raising activities (such as walks, dinners, or auctions), or work independently to raise money for a general donation.

The most important thing you can do to enlist support from those close to you is ask for help. Depending on what you are most comfortable doing, write letters, host dinners, or talk with people one on one. Share your personal challenges and explain why fund-raising is important in the fight against PD. Set a goal for yourself and work hard to achieve it. You can positively affect the lives of others living with PD.

Activism

Activism represents an opportunity to make your voice heard. Your local, state, and national leaders need to hear from people living with PD to encourage them to work for legislation that can benefit the PD community. You can join forces with a group like the Parkinson’s Action Network (PAN), an education and advocacy group representing the PD community in national and political affairs, or work independently to share your thoughts and concerns. Here are a few ways to include PD activism in your life:

- Know your members of Congress. The PAN Web site (www.parkinsonsaction.org) can provide you with lists of your elected representatives and their voting records on issues affecting the PD community. Write or call their offices to share your opinion about the issues important to you
• Meet with your members of Congress. You can call their offices to request meetings, or introduce yourself and your concerns at a town hall-type meeting

• Put your thoughts on paper. Inform others about the issues affecting the PD community by sending letters to the editor in local, state, or national publications

• Share your story. Talk to local civic groups, schools, or places of worship—PD advocacy groups can teach you how. Ask listeners to take action in specific ways, such as contacting members of Congress or donating money to PD advocacy groups for research or education initiatives. Your personal story is powerful. Sharing it with others is the best way to engage people in the fight against PD

Helping yourself and others through research and clinical trials

The medical research community has made tremendous progress in the treatment of PD. As a person affected by PD, your experiences and contributions can support promising research initiatives in understanding the disease, and help ensure that further opportunities are explored. If you’re interested in learning how you can serve as an advocate within the clinical research community, you may want to look into the Clinical Research Learning Institute (http://www.pdf.org/crli), sponsored by the Parkinson’s Disease Foundation. The institute holds a training program once a year to help people with PD learn how they can provide a patient’s perspective to the clinical research process. You can also see page 77 for clinical trials you may participate in; and pages 75-76 for more ways to get involved in helping yourself, your family, and other people with PD.
For family caregivers
Supporting your loved one and taking care of yourself

As a family caregiver, you will probably share in decisions about your loved one’s approach to PD management, seek information on his or her behalf, attend doctors’ appointments, or help with day-to-day activities. Although you probably think of yourself as a spouse, partner, child, friend, or neighbor of someone living with PD, you are, in fact, also a family caregiver. As such, you have rights and responsibilities that must be balanced to make the caregiver/recipient relationship work, and there are a few important things you can do to impact your loved one’s health and well-being, as well as your own.

- Attend doctor’s appointments with your loved one to take notes and help provide information to the physician

- Identify changes in your loved one’s symptoms or side effects, such as the onset of depression, abrupt worsening of slowness, or the onset of confusion (see the Watch for these sudden health changes Section on page 25). Make sure his or her physician is aware of these changes

- Help establish a treatment regimen, including the development of a schedule for medication dosing, exercise, therapy, etc.

- Assist with tasks of daily living, such as dressing and grooming, if needed

Caring for the caregiver

Eighty percent of people in the United States who require ongoing health care are cared for at home by a family caregiver. Your role is critical to the well-being of your loved one. It is also a weighty responsibility. Allow yourself to feel the emotions that may accompany your changing role in the relationship with your loved one and discuss them with others who may provide support.

You and your loved one must be candid about the reality that family caregivers need care too. The two of you are in a relationship, and you cannot meet your responsibilities if you neglect yourself physically, emotionally, or financially.

Most importantly, set realistic goals about the care you can—and cannot—provide for your loved one, based on your physical and mental strengths and limitations. It is important that you learn how to say “no.” Although you are
an essential and invaluable resource to your loved one. You need to take time for yourself and allow outside assistance. Know that, as a family caregiver, you make living with PD more manageable for your loved one.

Resources for caregivers
Taking care of your loved one is a great responsibility, but not one that you should take on alone. Many resources are available to assist you in your role as a family caregiver, including family and friends, support groups, counselors, professional caregivers, PD advocacy organizations (see pages 75-76 and 79 for listings), and the National Family Caregivers Association (www.thefamilycaregiver.org). When someone offers to help, accept their offer and delegate specific tasks to them. Don’t be afraid to ask for help when you need it or seek assistance from professionals.

10 TIPS FOR FAMILY CAREGIVERS*

- Caregiving is a job and relief is your earned right. Reward yourself with relief breaks often
- Watch out for signs of depression in yourself and don’t delay in getting professional help when you need it
- When people offer to help, accept the offer and suggest specific things they can do
- Educate yourself about your loved one’s condition and how to communicate effectively with doctors
- There’s a difference between caring and doing. Be open to technologies and ideas that promote your loved one’s independence
- Trust your instincts. Most of the time they’ll lead you in the right direction
- Caregivers often do a lot of lifting, pushing, and pulling. Be good to your back
- Grieve for your losses, and then allow yourself to dream new dreams
- Seek support from other caregivers. There is great strength in knowing you are not alone
- Stand up for your rights as a caregiver and a citizen

*Adapted with permission from 10 Tips for Family Caregivers, National Family Caregivers Association. Available in English and Spanish.
I was diagnosed with PD at the age of 46. Since then, I don’t feel like I’ve wasted one minute—traveling across the country, meeting others with PD, and talking to people who can help influence the fight for a cure.

It wasn’t always that way for me, though. When I went to my first support group meeting, I thought, “What am I doing here?” I felt like I didn’t belong. I later realized that not only could they help me, but I also learned to help them through encouragement. I learned there are many others out there dealing with the same thing.

When I turned 50 last year, my friends encouraged me to have a party. I didn’t want to, but I realized there might be an opportunity to bring people together for a cure. I asked guests to forego gifts in lieu of a donation to the Michael J. Fox Foundation. We raised more than $14,000 for the foundation at the party, and I was able to donate $500 more to the American Parkinson Disease Association. I actually got to meet Michael J. Fox, and it was one of the most memorable moments of my life.

I’m hoping to continue the tradition again this year. I want to help find a cure for this and help others. The best way for me to do that is to continue to support the organizations that hopefully will one day find a cure.

Ralph Sliwa
Norridge, Illinois
Resources
Parkinson’s disease advocacy, support, and community

American Parkinson Disease Association Inc.
www.apdaparkinson.org
800-223-2732
135 Parkinson Ave
Staten Island, NY 10305

The Michael J. Fox Foundation for Parkinson’s Research
www.michaeljfox.org
800-708-7644
Church Street Station
PO Box 780
New York, NY 10008-0780

National Parkinson Foundation, Inc.
www.parkinson.org
800-327-4545
1501 NW 9th Ave/Bob Hope Road
Miami, FL 33136-1494

The Parkinson Alliance
www.parkinsonalliance.net
800-579-8440
PO Box 308
Kingston, NJ 08528-0308

Parkinson’s Action Network
www.parkinsonsaction.org
800-850-4726
1025 Vermont Ave NW, Suite 1120
Washington, DC 20005

Parkinson’s Disease Foundation
www.pdf.org
800-457-6676
1359 Broadway, Suite 1509
New York, NY 10018
Parkinson’s disease advocacy, support, and community (continued)

We Move
www.wemove.org
204 West 84th St
New York, NY 10024

Movement Disorder Society
www.movementdisorders.org
414-276-2145
555 E Wells St, Suite 1100
Milwaukee, WI 53202-3823

The Parkinson’s Institute and Clinical Center
www.theipi.org
800-655-2273
675 Almanor Ave
Sunnyvale, CA 94085-2935

www.parkinsonshealth.com — Tips and tools for living with PD, information on symptoms and treatments, and animated illustrations related to PD. Also offers registration for a free subscription to Life in Balance—A Newsletter for People and Families Living with PD™.

www.azilect.com — Helpful PD information for patients, frequent news updates, plus information about AZILECT® (rasagiline tablets).*


*Please see important safety information on pages 44-45.
Professional medical associations

American Academy of Neurology
www.aan.com
800-879-1960
1080 Montreal Ave
St. Paul, MN 55116

American Neurological Association
www.aneuroa.org
952-545-6284
5841 Cedar Lake Rd, Suite 204
Minneapolis, MN 55416

National Institute of Neurological Disorders and Strokes
www.ninds.nih.gov
800-352-9424
NIH Neurological Institute
PO Box 5801
Bethesda, MD 20824

Clinical trials

www.centerwatch.com (866-219-3440) — Lists of PD clinical trials by state from CenterWatch.

www.clinicaltrials.gov — General information from the National Institutes of Health (NIH) about clinical trials.


www.pdtrials.org — Information about clinical trials in PD from the Parkinson’s Disease Foundation working in collaboration with other Parkinson’s organizations.
Insurance, Medicare, and Medicaid


www.medicarerights.org (800-333-4114) — Independent source of Medicare information and assistance in the US from the Medicare Rights Center.

www.patientadvocate.org (800-532-5274) — Information on getting answers from, and negotiating claims with, private insurance companies from the Patient Advocate Foundation.

www.togetherrxaccess.com (800-444-4106) — Information on a prescription savings card for those patients not already covered by Medicare.

Medical records (may entail out-of-pocket cost)


www.peoplechart.com — Helps patients collect, organize, and securely distribute copies of their medical records, anytime and anywhere.

Adaptive equipment

www.abledata.com (800-227-0216) — Information from the National Institute on Disability and Rehabilitation Research on assistive technology.


www.nscd.org (970-726-1540) — Information on adaptive athletics from the National Sports Center for the Disabled.

www.nrrts.org (800-976-7787) — National Registry of Rehabilitation Technology Suppliers provides special expertise on fitting wheelchairs or other mobility equipment.
Alternative treatments

www.amtamassage.org (877-905-2700) — Information on massage therapy and relaxation techniques from the American Massage Therapy Association.


www.medicalacupuncture.org (310-364-0193) — Information about acupuncture from the American Academy of Medical Acupuncture.


Exercise, nutrition, and sleep

www.acefitness.org (888-825-3636) — Information on the importance of physical activity in maintaining good health from the American Council on Exercise.

www.nutrition.gov — Contains recommended daily allowances and nutritional content of many foods from the Department of Agriculture.

www.sleepfoundation.org (202-347-3471) — Information on the importance of sleep for optimal health from the National Sleep Foundation.

Family caregiving

www.caregiver.org (800-445-8106) — Information, resources, and state-by-state breakdown of public programs for family caregivers from the Family Caregiver Alliance.

www.thefamilycaregiver.org (800-896-3650) — Education, support, and advocacy from those who walk in a family caregiver’s shoes. Information and resources to assist your family caregiver from the National Family Caregivers Association.

www.caregiving.com — An online support community for family caregivers where they can share real-life experiences and ideas.
Who would have ever believed the words, “You have Parkinson’s disease at the age of 33”? I sure didn’t want to. I had a brand-new baby at home, a good job, and my independence.

I am here to tell you, though, it is going to be okay. Yes, it took me some time to come to the realization that I have a disease that will, in time, change some aspects of my life. The key to accepting that was finding I have other talents and new avenues to walk down.

Having PD has brought out my creative side. I have found I really enjoy writing poems. Photography is also a fun hobby I have more time for now. My true passion, though, is being a mom to my 5-year-old daughter. She keeps me on my toes at all times, helps me stay active, and gives me a desire to keep pushing forward. She puts a fire in my heart to kick PD. At night’s end, tired and worn, I tuck her into bed and thank God for sharing her with me. The unconditional love of a child is truly priceless.

Find that inner place that brings you peace and puts a smile in your heart and on your face, then embrace and enjoy it. You deserve to be happy. Nothing can stand in your way and keep you down, except you.

Kelly Maurer
Perrysburg, Ohio
Glossary of PD terms*

**Adaptive equipment:** Tools, appliances, equipment, and related devices that are used to assist people with physical disabilities to complete activities of daily living.

**Adjunct therapy:** Use of treatments in addition to the primary mode of treatment, for example, the addition of a second PD therapy to either carbidopa/levodopa or another PD drug therapy.

**Akinesia** [A-kin-NEE-juh]: Lack of or loss of the ability to initiate movement.

**Bradykinesia** [bray-dee-kin-NEE-juh]: Slowness of movement.

**Bradyphrenia** [bray-dee-FREEN-ya]: Slowness of thinking.

**Clinical trial:** A research study to answer specific questions about new medicines or new ways of using existing treatments. Also called medical research, research studies, or clinical studies, clinical trials are used to determine whether new drugs or treatments are both safe and effective.

**Deep brain stimulation (DBS):** Delivery of an electrical signal to targeted areas in the brain that control movement using a surgically implanted, battery-operated medical device. This blocks the abnormal nerve signals that cause tremor and PD symptoms.

**Dopamine:** A neurotransmitter, or chemical messenger, that transports signals to the parts of the brain that control movement.

**Dosing schedule:** The number of times a day that a medicine is taken and the amount of drug taken in each dose; may also include the clock time during the day that each dose is taken.

**Dosing strength:** The number of milligrams or grams of medicine in a tablet, pill, or capsule. Also called “dosage strength.”

**Dyskinesia** [dis-kih-NEE-juh]: Abnormal, random, twisting, turning, involuntary movement, usually seen in the arms, legs, head, and trunk.

**Dysphagia** [dis-FAY-juh]: Difficulty swallowing.

*Adapted with permission from A Glossary for Parkinson’s Disease, Parkinson’s Disease Foundation, Inc.*
**Dystonia** [dis-TOH-nee-uh]: Sustained involuntary muscle contraction.

**Freezing, or freezing of gait (FOG):** The sudden but temporary inability to move the legs and feet when walking; the sense that one’s feet are glued to the floor.

**Hallucinations:** An abnormal sense perception unrelated to real events, such as seeing or hearing people or animals that are not there.

**Hoehn & Yahr** [HONE and YAR] Scale: A 5-stage scale used by physicians and researchers to rate the level of disability and the severity of the symptoms caused by PD.

**Hypophonia** [hy-po-FO-nee-uh]: Reduced speech volume.

**Micrographia** [my-kro-GRAF-ee-uh]: Small, cramped handwriting.

**Monotherapy:** The use of a single therapy in the treatment of a disease.

**Motor symptoms:** Symptoms of PD affecting movement.

**Neuron:** A cell that conducts impulses and carries information from one part of the brain to another.

**Nonmotor symptoms:** PD symptoms unrelated to movement.

**“Off” time:** Time when PD medications fail to control symptoms. Commonly experienced before a dose of medication has “kicked in,” or when an earlier dose has worn off.

**“On” time:** Time when PD medications successfully control symptoms.

**“On” time with dyskinesia:** A period of time when medication controls PD symptoms but also causes uncontrolled twisting, turning movements, called dyskinesia.

**On-off phenomenon:** Unpredictable response to a dose of levodopa, in which rapid switches are made between adequate symptom control (“on” time) and inadequate symptom control (“off” time).

**Parkinsonism:** A collection of symptoms in which a patient has a combination of tremor, stiffness, slowness, and balance problems. The most common cause of parkinsonism is PD, but it can also be caused by other illnesses or certain medications.
**Parkinson’s disease**: Parkinson’s disease is a chronic progressive neurological disease that affects a small area of nerve cells (neurons) in an area of the brain known as the substantia nigra. These cells normally produce dopamine, a chemical (neurotransmitter) that transmits signals between areas in the brain that, when working normally, coordinate smooth and balanced muscle movement. Parkinson’s disease causes these nerve cells to die, and as a result, body movements are affected.

**Resting tremor**: A rhythmic shaking that is more obviously seen when the affected body part is at rest.

**Restless leg syndrome (RLS)**: A condition that produces an intense, often irresistible urge to move the legs because of unpleasant sensations, usually while trying to sleep. Moving the legs sometimes provides temporary relief.

**Rigidity**: Stiffness in the muscles or resistance to movement.

**Substantia nigra** [sub-STAN-shuh-NIGH-gruh]: One of the movement control centers in the brain where loss of dopamine-producing cells triggers PD symptoms.

**Unified Parkinson’s Disease Rating Scale (UPDRS)**: A scale used by physicians to assign a numerical rating to the various symptoms of PD and to determine the severity of the disease. Used most often in clinical trials in order to gauge the effectiveness of a treatment by measuring UPDRS scores at the initiation of a trial and again after administration of a new treatment.
Keeping track of information
On the following pages, you will find a checklist for things to keep in mind when you’re talking to your doctor. You’ll also find a list of important things related to yourself and your PD—such as a list of emergency contacts, and your past and current medications—that can help you in your PD management. Having that kind of information written on a card or paper can be helpful to you and your family caregivers, should any emergency arise.

Developing an effective relationship with your physician and other health care providers

Use the checklist below to evaluate your relationship with your physician. If your doctor is not currently meeting your needs or expectations, talk with him or her about changes that could improve your level of satisfaction. You are a consumer of your health care, and you should work to ensure that you are receiving the quality of care you deserve.

☐ Are you comfortable with your doctor? Does he or she make you feel at ease?

☐ Does your doctor understand your personal priorities? Does he or she take them into consideration when making recommendations about your treatment?

☐ Does your doctor listen to your concerns and take them seriously?

☐ Does your doctor ask you about the impact of symptoms and side effects on your daily life?

☐ Is your doctor respectful of your opinion and the opinion of your family caregiver?

☐ Does your doctor see you and your family caregiver as equal partners in the management of your PD?
Developing an effective relationship with your physician and other health care providers (continued)

☐ Does your doctor explain his or her recommendations in a way that is easy to understand?

☐ Does your doctor give you thorough instructions regarding medications or other treatment options?

☐ Does your doctor recommend nondrug treatments (such as exercise, diet, and attention to emotional well-being) in addition to medications?

☐ Does your doctor inquire about aspects of your health that fall outside of his or her specialty?

☐ Does your doctor talk to, or share files with, your other physicians?

☐ Is your doctor or a member of his or her staff available to answer your questions or address your concerns between office visits?

☐ Does your doctor arrive for your appointments in a timely manner?

☐ Does your doctor allow enough time for a thorough examination and to answer your questions?

☐ Does your doctor educate you about PD on an ongoing basis? Does he or she refer you to additional resources or support groups?

☐ Does your doctor encourage you to get a second opinion or refer you to a specialist when appropriate?

☐ Does your doctor stay up-to-date on research findings about PD and new treatment options?

☐ Does your doctor inform you about clinical trials in which you may be eligible to participate?
Creating written lists of information about you and your PD

Having your personal information and details about your medical history close at hand can be helpful to you, your family caregivers, and others who may become involved in your care. You may want to consider keeping a card or a written list of important information in your wallet or purse. This list could include:

- Your name, address, phone numbers, emergency contacts, and insurance policy details
- A summary of current medical issues and conditions, including your PD, with your date of diagnosis for each
- A summary of your family health history
- Current and past prescription medications for PD or other conditions, with the medication names, dosing strengths, and dosing schedules
- Information on any herbal or dietary supplements, or over-the-counter medications you have taken or take now, plus how often you take them
- Allergies to food or medications
- A list of your health care team members, where they practice, and their phone numbers
- A description of your functional capabilities, such as need for help when you’re walking
- Religious or cultural considerations, such as scheduled prayer times or dietary restrictions
- Information about a living will or other directives regarding your health care, plus contact information for the person who holds those documents (such as a family member or attorney)

You may also want to keep a diary of any symptoms or side effects you experience, so that you can share it with your health care provider and help the two of you determine the best treatment for you.
Appendix

Keep in touch with activities you love with AZILECT® (rasagiline tablets).

- Effective for newly diagnosed patients
- Provides additional symptom relief and decreases “off” time for patients who take carbidopa/levodopa
- Can be taken with other PD therapies
- Convenient—just one pill, once a day, always
- Well tolerated

For more information, visit www.azilect.com.

The medications listed in Moving Forward™ do not constitute an express or implied endorsement by any of the consultants.
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AZILECT® safely and effectively. See full prescribing information for AZILECT®:

AZILECT® (rasagiline mesylate) Tablets for Oral Use
Initial U.S. Approval: 2006

RECENT MAJOR CHANGES
Dosage and Administration 12/2009
Contraindications 12/2009
Warnings and Precautions 12/2009

INDICATIONS AND USAGE
AZILECT is indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease as initial monotherapy and as adjunct therapy to levodopa. (1)

DOSAGE AND ADMINISTRATION
• Monotherapy: AZILECT 1 mg once daily (2.1)
• As adjunct to levodopa: AZILECT 0.5 mg once daily. Dose increase to 1 mg daily as required for sufficient clinical response. (2.2)
• Patients with mild hepatic impairment: AZILECT 0.5 mg once daily should not be exceeded. AZILECT should not be used in patients with moderate or severe hepatic impairment (2.3)
• AZILECT has not been studied in patients with severe renal impairment (2.4)
• Patients taking ciprofloxacin or other CYP1A2 inhibitors: AZILECT 0.5 mg once daily should not be exceeded. (2.5)

DOSAGE FORMS AND STRENGTHS
• AZILECT 0.5 mg tablets (containing, as the active ingredient, rasagiline mesylate equivalent to 0.5 mg of rasagiline base) (3)
• AZILECT 1 mg tablets (containing, as the active ingredient, rasagiline mesylate equivalent to 1 mg of rasagiline base) (3)

CONTRAINDICATIONS
• Concomitant use of:
  - meperidine, tramadol, methadone or propoxyphene (4.1)
  - dextromethorphan, St. John’s wort or cyclobenzaprine (4.2)
  - other MAO inhibitors (selective or non-selective) (4.3)

WARNINGS AND PRECAUTIONS
• Risk of severe CNS toxicity (serotonin syndrome) when AZILECT is combined with antidepressants. (5.1)
• Concomitant use of ciprofloxacin or other CYP1A2 inhibitors: Increase in rasagiline plasma concentrations. 0.5 mg rasagiline once daily should not be exceeded (5.2)
• Patients with hepatic impairment: Increase in rasagiline plasma concentrations. Limit dose to 0.5 mg rasagiline in mild hepatic impairment. AZILECT should not be used in patients with moderate or severe hepatic impairment (5.3)
• Risk for Hypertensive Crisis and nonselective MAO inhibition above the recommended Doses (5.4)
• Melanoma (5.4)
• AZILECT may cause lower blood pressure, especially postural hypotension (5.7) or increase blood pressure in different patients (5.8)
• AZILECT may cause or exacerbate hallucinations or potentially other manifestations of psychotic-like behavior (5.9)

ADVERSE REACTIONS
• Most common adverse reactions (treatment difference ≥ 3% greater than placebo); with monotherapy: flu syndrome, arthralgia, depression, dyspepsia. (6.1)
• Most common adverse reactions (treatment difference ≥ 3% greater than placebo); when used as adjunct to levodopa: dyskinesia, accidental injury, weight loss, postural hypotension, vomiting, anorexia, arthralgia, abdominal pain, nausea, constipation, dry mouth, rash, abnormal dreams, fall. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact TEVA at 1-800-221-4026 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
• Meperidine: Risk of serious, sometimes fatal reactions from serotonin syndrome. See also Contraindications. (7.1)
• Dextromethorphan: Risk of psychosis episodes or bizarre behavior. See also Contraindications. (7.2)
• MAO inhibitors: Risk of non-selective MAO inhibition and hypertensive crisis. See also Contraindications. (7.4)
• Antidepressants (SSRIs, SNRIs, tricyclic, tetracyclic, or triazolopyridine): Concomitant use not recommended. (7.5)
• Levodopa: See also Warnings and Precautions. (7.6)
• Ciprofloxacin and Other CYP1A2 Inhibitors: Increased rasagiline plasma levels possible. Increased risk of adverse events. See also Dosage and Administration and Warnings and Precautions.(7.7)

USE IN SPECIFIC POPULATIONS
• Pregnancy: AZILECT should be used only if the potential benefit justifies the potential risk to the fetus. (8.1)
• Nursing mothers: Rasagiline inhibits prolactin secretion and may inhibit milk secretion. It is not known whether rasagiline is excreted in human milk. Use with caution. (8.3)
• Hepatic impairment: Rasagiline plasma concentrations may be increased. See also Dosage and Administration and Warnings and Precautions. (8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2009
FULL PRESCRIBING INFORMATION: CONTENTS*

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AZILECT® (rasagiline tablets)

1 INDICATIONS AND USAGE
AZILECT (rasagiline tablets) is indicated for the treatment of the signs and symptoms of idiopathic Parkinson’s disease as initial monotherapy and as adjunct therapy to levodopa.

The effectiveness of AZILECT was demonstrated in patients with early Parkinson’s disease who were receiving AZILECT as monotherapy and who were not receiving any concomitant dopaminergic therapy. The effectiveness of AZILECT as adjunct therapy was demonstrated in patients with Parkinson’s disease who were treated with levodopa.

2 DOSAGE AND ADMINISTRATION
AZILECT is a selective inhibitor of monoamine oxidase (MAO)-B at recommended doses of 0.5 or 1 mg daily. Dietary tyramine restriction is not ordinarily required with recommended doses of AZILECT. However, certain foods (e.g., aged cheeses, such as Stilton cheese) may contain very high amounts (i.e., > 150 mg) of tyramine and could potentially cause a hypertensive “cheese” reaction in patients taking AZILECT even at the recommended dose due to mild increased sensitivity to tyramine. The selectivity for inhibiting MAO-B diminishes in a dose-related manner as the dose is progressively increased above the recommended daily dose [see Warnings and Precautions (5.4), Clinical Pharmacology (12.3), and Information for Patients (17.3)].

2.1 Monotherapy
The recommended AZILECT dose for the treatment of Parkinson’s disease patients is 1 mg administered orally once daily.

2.2 Adjunctive Therapy
The recommended initial dose is 0.5 mg administered orally once daily. If a sufficient clinical response is not achieved, the dose may be increased to 1 mg administered once daily.

Change of Levodopa Dose in Adjunct Therapy
When AZILECT is used in combination with levodopa, a reduction of the levodopa dosage may be considered based upon individual response. During the controlled trials of AZILECT as adjunct therapy to levodopa, levodopa dosage was reduced in some patients. In clinical studies, dosage reduction of levodopa was allowed within the first 6 weeks if dopaminergic side effects, including dyskinesias and hallucinations, emerged. In Study 1, levodopa dosage reduction occurred in 8% of patients in the placebo group and in 16% and 17% of patients in the 0.5 mg/day and 1 mg/day rasagiline groups, respectively. In those patients who had levodopa dosage reduced, the dose was reduced on average by about 7%, 9%, and 13% in the placebo, 0.5 mg/day, and 1 mg/day groups, respectively. In Study 2, levodopa dosage reduction occurred in 6% of patients in the placebo group and in 9% in the rasagiline 1 mg/day group. In patients who had their levodopa dosage reduced, the dose was reduced on average by about 13% and 11% in the placebo and the rasagiline groups, respectively.

2.3 Patients with Hepatic Impairment
AZILECT plasma concentrations will increase in patients with hepatic impairment. Patients with mild hepatic impairment should use 0.5 mg daily of AZILECT. AZILECT should not be used in patients with moderate or severe hepatic impairment [see Warnings and Precautions (5.3), Use in Specific Populations (8.6), and Clinical Pharmacology (12.3)].

2.4 Patients with Renal Impairment
Dose adjustment of AZILECT is not required for patients with mild or moderate renal impairment because AZILECT plasma concentrations are not increased in patients with moderate renal impairment. Rasagiline has not been studied in patients with severe renal impairment.

2.5 Patients Taking Ciprofloxacin or Other CYP1A2 Inhibitors
Rasagiline plasma concentrations are expected to double in patients taking concomitant ciprofloxacin and other CYP1A2 inhibitors. Therefore, patients taking concomitant ciprofloxacin or other CYP1A2 inhibitors should use 0.5 mg daily of AZILECT [see Warnings and Precautions (5.2), Drug Interactions (7.7), and Clinical Pharmacology (12.3)].

3 DOSAGE FORMS AND STRENGTHS
AZILECT 0.5 mg Tablets: White to off-white, round, flat, beveled tablets, debossed with “GIL 0.5” on one side and plain on the other side containing, as the active ingredient, rasagiline mesylate equivalent to 0.5 mg of rasagiline base.

AZILECT 1 mg Tablets: White to off-white, round, flat, beveled tablets, debossed with “GIL 1” on one side and plain on the other side containing, as the active ingredient, rasagiline mesylate equivalent to 1 mg of rasagiline base.

4 CONTRAINDICATIONS
4.1 Meperidine and Certain Other Analgesics
AZILECT is contraindicated for use with meperidine. Serious adverse reactions have been precipitated with concomitant use of meperidine (e.g., Demerol and other tradenames) and MAO inhibitors (MAOIs) including selective MAO-B inhibitors. These adverse reactions are often described as “serotonin syndrome”, a potentially serious condition, which can result in death. Typical clinical signs and symptoms include behavioral and cognitive/mental status changes (e.g., confusion, hypomania, hallucinations, agitation, delirium, headache, and coma), autonomic effects (e.g., syncope, shivering, sweating, high fever/hyperthermia, hypertension, hypotension, tachycardia, nausea, diarrhea), and somatic effects (e.g., muscular rigidity, myoclonus, muscle twitching, hyperreflexia manifested by clonus, and tremor). At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with meperidine.
For similar reasons, AZILECT should not be administered with the analgesic agents tramadol, methadone, and propoxyphene.

In the post-marketing period, serotonin syndrome has been reported in a patient erroneously treated with a higher than recommended dose of AZILECT (4 mg daily) and tramadol.

### 4.2 Other Drugs

AZILECT should not be used with the antitussive agent dextromethorphan. The combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior. AZILECT is also contraindicated for use with St. John's wort, and cyclobenzaprine (a tricyclic muscle relaxant).

### 4.3 MAO Inhibitors

AZILECT should not be administered along with any other MAO inhibitor (selective or non-selective) because of the increased risk of non-selective MAO inhibition that may lead to a hypertensive crisis. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with any MAO inhibitor.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Co-administration with Antidepressants

Severe CNS toxicity associated with hyperpyrexia has been reported with the combined treatment of an antidepressant (e.g., selective serotonin reuptake inhibitors-SSRIs, serotonin-norepinephrine reuptake inhibitors-SNRIs, tricyclic antidepressants, tetracyclic antidepressants, triazolopyridine antidepressants) and a non-selective MAOI (e.g., phenelzine, tranylcypromine) or selective MAO-B inhibitors, such as selegiline (Eldepryl) and rasagiline (AZILECT). These adverse reactions are often described as "serotonin syndrome" which can result in death. In the post-marketing period, non-fatal cases of serotonin syndrome have been reported in patients treated with antidepressants concomitantly with AZILECT.

The symptoms of serotonin syndrome have included behavioral and cognitive/mental status changes (e.g., confusion, agitation, delirium, headache, and coma), autonomic effects (e.g., syncope, shivering, sweating, high fever/hyperthermia, hypertension, tachycardia, nausea, diarrhea), and somatic effects (e.g., muscular rigidity, myoclonus, muscle twitching, hyperreflexia manifested by clonus, and tremor).

AZILECT clinical trials did not allow concomitant use of fluoxetine or fluvoxamine with AZILECT, but the following antidepressants and doses were allowed in the AZILECT trials: amitriptyline ≤ 30 mg/daily, trazodone ≤ 100 mg/daily, citalopram ≤ 20 mg/daily, sertraline ≤ 100 mg/daily and paroxetine ≤ 30 mg/daily.

Although a small number of rasagiline-treated patients were concomitantly exposed to antidepressants (tricyclics n=115; SSRIs n=141), the exposure, both in dose and number of subjects, was not adequate to rule out the possibility of an untoward reaction from combining these agents. Furthermore, because the mechanisms of these reactions are not fully understood, it seems prudent, in general, to avoid the combination of AZILECT with any antidepressant. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with a SSRI, SNRI, tricyclic, tetracyclic, or triazolopyridine antidepressant. Because of the long half lives of certain antidepressants (e.g., fluoxetine and its active metabolite), at least five weeks (perhaps longer, especially if fluoxetine has been prescribed chronically and/or at higher doses) should elapse between discontinuation of fluoxetine and initiation of AZILECT [see Drug Interactions (7.5)].

#### 5.2 Ciprofloxacin and Other CYP1A2 Inhibitors

Rasagiline plasma concentrations may increase up to 2 fold in patients using concomitant ciprofloxacin and other CYP1A2 inhibitors [see Dosage and Administration (2.5), Drug Interactions (7.7), and Clinical Pharmacology (12.3)].

#### 5.3 Hepatic Impairment

Rasagiline plasma concentration may increase in patients with mild (up to 2 fold, Child-Pugh score 5-6), moderate (up to 7 fold, Child-Pugh score 7-9), and severe (Child-Pugh score 10-15) hepatic impairment. Patients with mild hepatic impairment should be given the dose of 0.5 mg/day. AZILECT should not be used in patients with moderate or severe hepatic impairment [see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)].

#### 5.4 Risk for Hypertensive Crisis and Nonselective Monoamine Oxidase Inhibition

**Above The Recommended Doses**

AZILECT is a selective inhibitor of monoamine oxidase (MAO)-B at the recommended doses of 0.5 mg daily. AZILECT should not be used at daily doses exceeding 1 mg/day (or 0.5 mg/day for patients with mild hepatic impairment or in patients using concomitant ciprofloxacin or another CYP1A2 inhibitor) because of the risks of hypertensive crisis and other adverse reactions associated with nonselective inhibition of MAO [see Dosage and Administration (2), Drug Interactions (7.9), and Clinical Pharmacology (12.3)].

Dietary tyramine restriction is not ordinarily required with ingestion of most foods and beverages that may contain tyramine, during treatment with recommended doses of AZILECT. However, certain foods (e.g., aged cheeses, such as Stilton cheese) may contain very high amounts (i.e., > 150 mg) of tyramine and could potentially cause a hypertensive "cheese" reaction in patients taking AZILECT even at the recommended doses due to mild increased sensitivity to tyramine. Patients should be advised to avoid foods (e.g., aged cheese) containing a very large amount of tyramine while taking recommended doses of AZILECT because of the potential for large increases in blood pressure. Selectivity for inhibiting MAO-B diminishes in a dose-related manner as the dose is progressively increased above the recommended daily doses.

There were no cases of hypertensive crisis in the clinical development program associated with 1 mg daily rasagiline treatment, in which most patients did not follow dietary tyramine restriction.

Rare cases of hypertensive crisis have been reported in the post-marketing period in patients after ingesting unknown amounts of tyramine-rich foods while taking recommended doses of AZILECT.

#### 5.5 Melanoma

Epidemiological studies have shown that patients with Parkinson’s disease have a higher risk (2- to approximately 6-fold higher) of developing melanoma than the general population. Whether the increased risk observed was due to Parkinson’s disease or other factors, such as drugs used to treat Parkinson’s disease, is unclear.

For the reasons stated above, patients and providers are advised to monitor for melanomas frequently and on a regular basis. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g., dermatologists).
5.6 Dyskinesia
When used as an adjunct to levodopa, AZILECT may cause dyskinesia or potentiate dopaminergic side effects and exacerbate pre-existing dyskinesia (treatment-emergent dyskinesia occurred in about 18% of patients treated with 0.5 mg or 1 mg rasagiline as an adjunct to levodopa, and 10% of patients who received placebo as an adjunct to levodopa). Decreasing the dose of levodopa may ameliorate this side effect.

5.7 Lowering of Blood Pressure and Postural/Orthostatic Hypotension
In placebo controlled studies of AZILECT given in combination with levodopa, the incidence of postural hypotension consisting of a systolic blood pressure decrease (≥ 30 mm Hg) or a diastolic blood pressure decrease (≥ 20 mm Hg) after standing was 13.4% with AZILECT (1 mg/day) compared to 8.5% with placebo.

At the 1 mg dose, the frequency of orthostatic hypotension at any time during the study was approximately 44% for AZILECT vs 33% for placebo for mild to moderate systolic blood pressure decrements (≥ 20 mm Hg), 40% for AZILECT vs 33% for placebo for mild to moderate diastolic blood pressure decrements (≥ 10 mm Hg), 7% for AZILECT vs 3% for placebo for severe systolic blood pressure decrements (≥ 40 mm Hg), and 9% for AZILECT vs 6% for placebo for severe diastolic blood pressure decrements (≥ 20 mm Hg). There was also an increased risk for some of these abnormalities at the lower 0.5 mg daily dose and for an individual patient having mild to moderate or severe postural hypotension for both systolic and diastolic blood pressure.

Clinical trial data further suggest that postural hypotension occurs most frequently in the first two months of AZILECT treatment and tends to decrease over time.

Some patients treated with AZILECT experienced a mildly increased risk for significant decreases in blood pressure unrelated to standing but while supine.

The risk for post-treatment hypotension (e.g., systolic < 90 or diastolic < 50 mm Hg) combined with a significant decrease from baseline (e.g., systolic > 30 or diastolic > 20 mm Hg) was higher for AZILECT 1 mg (3.2%) compared to placebo (1.3%).

There was no clear increased risk for lowering of blood pressure or postural hypotension associated with AZILECT 1 mg/day as monotherapy.

When used as an adjunct to levodopa, postural hypotension was also reported as an adverse reaction in approximately 6% of patients treated with 0.5 mg rasagiline, 9% of patients treated with 1 mg rasagiline and 3% of patients treated with placebo. Postural hypotension led to drug discontinuation and premature withdrawal from clinical trials in about 0.7% of patients treated with rasagiline 1 mg/day, no patients treated with rasagiline 0.5 mg/day and no placebo-treated patients.

5.8 Elevation of Blood Pressure
In studies in which AZILECT (1 mg/day) was given in conjunction with levodopa, AZILECT produced an increased incidence of a significant, high blood pressure (e.g., systolic > 180 or diastolic > 100 mm Hg) of 4% compared to 3% for placebo. The risk for developing post-treatment high blood pressure (e.g., systolic > 180 or diastolic > 100 mm Hg) combined with a significant increase from baseline (e.g., systolic > 30 or diastolic > 20 mm Hg) was higher for AZILECT 1 mg (2%) compared to placebo (1%).

There was no increased frequency of the incidence of hypertension as an adverse reaction in the adjunctive treatment pivotal trials for AZILECT treatment vs placebo.

There was no observed increased risk for increasing blood pressure or high blood pressure (based upon various measurements and analyses) or for the development of hypertension as an adverse reaction in the monotherapy study for 1 mg daily AZILECT treatment (vs placebo).

5.9 Hallucinations/Psychotic-Like Behavior
In the monotherapy study, hallucinations were reported as an adverse event in 1.3% of patients treated with 1 mg rasagiline and in 0.7% of patients treated with placebo. In the monotherapy trial, hallucinations led to drug discontinuation and premature withdrawal from clinical trials in 1.3% of the 1 mg rasagiline-treated patients and in none of the placebo-treated patients.

When used as an adjunct to levodopa, hallucinations were reported as an adverse reaction in approximately 5% of patients treated with 0.5 mg/day AZILECT, 4% of patients treated with 1 mg/day AZILECT and 3% of patients treated with placebo. Hallucinations led to drug discontinuation and premature withdrawal from clinical trials in about 1% of patients treated with 0.5 mg/day or 1 mg/day rasagiline and none of the placebo-treated patients.

Patients should be informed of the possibility of developing hallucinations and instructed to report them to their health care provider promptly should they develop.

Patients with a major psychotic disorder should ordinarily not be treated with AZILECT because of the risk of exacerbating the psychosis with an increase in central dopaminergic tone. In addition, many treatments for psychosis that decrease in central dopaminergic tone may decrease the effectiveness of AZILECT.

AZILECT administration may cause or exacerbate psychotic-like behavior based upon post-marketing reports. This adverse reaction has been reported with many anti-Parkinsonian drugs that increase central dopaminergic tone. This abnormal behavior has been exhibited by one or more of a variety of manifestations including paranoia, confusional state/confusion, psychotic disorder, agitation, delusion, and hallucinations.

5.10 Withdrawal-Emergent Hyperpyrexia and Confusion
A symptom complex resembling neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in drugs that increase central dopaminergic tone. [See Dosage and Administration (2.2)].

Withdrawal emergent hyperpyrexia was not reported in the AZILECT clinical development program.

5.11 Laboratory Tests
No specific laboratory tests are required for the treatment of patients on AZILECT.

6 ADVERSE REACTIONS
6.1 Clinical Studies Experience
During the clinical development of AZILECT, 1361 Parkinson’s disease patients received rasagiline as initial monotherapy or as adjunct therapy to levodopa. As these two populations differ, not only in the adjunct use of levodopa during rasag-
line treatment, but also in the severity and duration of their disease, they may have differential risks for various adverse re-
actions. Therefore, most of the adverse reactions data in this section are presented separately for each population.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clini-
tical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates
of adverse reactions observed in practice.

Patients Receiving AZILECT as Initial Monotherapy Treatment

Adverse Reactions Leading to Discontinuation in Controlled Clinical Studies

In the double-blind, placebo-controlled trials conducted in patients receiving AZILECT as monotherapy, approxi-
mately 5% of the 149 patients treated with rasagiline discontinued treatment due to adverse reactions compared to 2% of
the 151 patients who received placebo.

The only adverse reaction that led to the discontinuation of more than one patient was hallucinations.

Adverse Reaction Incidence in Controlled Clinical Studies

The most commonly observed adverse reactions were those in which the treatment difference for the incidence in
AZILECT-treated patients was ≥ 3% greater than the incidence in the placebo-treated patients and included flu syndrome,
arthralgia, depression, and dyspepsia. Table 1 lists treatment-emergent adverse reactions that occurred in ≥ 2% of pa-
tients receiving AZILECT as monotherapy participating in the double-blind, placebo-controlled trial and were numerically
more frequent than in the placebo group.

Table 1. Treatment-Emergent* Adverse Reactions in AZILECT 1 mg-Treated Monotherapy Patients

<table>
<thead>
<tr>
<th>Placebo-Controlled Studies Without Levodopa Treatment</th>
<th>AZILECT 1 mg (N=149)</th>
<th>Placebo (N=151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Patients</td>
<td>% of Patients</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Depression</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Fall</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Flu syndrome</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Fever</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Arthritis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Malaise</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Neck Pain</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Vertigo</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

*Incidence ≥ 2% in AZILECT 1 mg group and numerically more frequent than in placebo group

Other events of potential clinical importance reported by 1% or more of patients receiving AZILECT as monoth-
erapy, and at least as frequent as in the placebo group, in descending order of frequency include: dizziness, diarrhea, chest
pain, albuminuria, allergic reaction, alopecia, angina pectoris, anorexia, asthma, hallucinations, impotence, leukopenia, li-
bido decreased, liver function tests abnormal, skin carcinoma, syncope, vesiculobullous rash, vomiting.

There were no significant differences in the safety profile based on age or gender.

Patients Receiving AZILECT as Adjunct to Levodopa Therapy

Adverse Reactions Leading to Discontinuation in Controlled Clinical Studies

In a double-blind, placebo-controlled trial (Study 1) conducted in patients treated with AZILECT as adjunct to levo-
dopa therapy, approximately 9% of the 164 patients treated with AZILECT 0.5 mg/day and 7% of the 149 patients treated
with AZILECT 1 mg/day discontinued treatment due to adverse reactions compared to 6% of the 159 patients who received
placebo. The adverse reactions that led to discontinuation of more than one rasagiline-treated patient were: diarrhea,
weight loss, hallucination, and rash. Adverse event reporting was considered more reliable for Study 1 than for the sec-
ond controlled trial (Study 2); therefore only the adverse event data from Study 1 are presented in this section of labeling.

Adverse Reactions: Incidence in Controlled Clinical Studies

The most commonly observed adverse reactions were those in which the treatment difference for the incidence in
AZILECT-treated patients (n=149) was ≥ 3% greater than the incidence in the placebo-treated patients (n=159) and in-
cluded dyskinesia, accidental injury, weight loss, postural hypotension, vomiting, anorexia, arthralgia, abdominal pain,
nausea, constipation, dry mouth, rash, abnormal dreams, and fall.

Table 2 lists treatment-emergent adverse reactions that occurred in ≥ 2% of patients treated with AZILECT 1 mg/day
as adjunct to levodopa therapy participating in the double-blind, placebo-controlled trial (Study 1) and that were numeri-
cally more frequent than the placebo group. The table also shows the rates for the 0.5 mg group in Study 1.
### Table 2. Incidence of Treatment-Emergent* Adverse Reactions in Patients Receiving AZILECT as Adjunct to Levodopa Therapy in Study 1

<table>
<thead>
<tr>
<th></th>
<th>AZILECT 1 mg + Levodopa (N=149)</th>
<th>AZILECT 0.5 mg + Levodopa (N=164)</th>
<th>Placebo + Levodopa (N=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>18</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Accidental injury</td>
<td>12</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Nausea</td>
<td>12</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Headache</td>
<td>11</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Fall</td>
<td>11</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Weight loss</td>
<td>9</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Constipation</td>
<td>9</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>9</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>6</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Rash</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Somnolence</td>
<td>6</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Anorexia</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Abnormal dreams</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>4</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Ataxia</td>
<td>3</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>3</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Infection</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Neck pain</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sweating</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Tenosynovitis</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dystonia</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hernia</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Myasthenia</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

*Incidence ≥ 2% in AZILECT 1 mg group and numerically more frequent than in placebo group.

Several of the more common adverse reactions seemed dose-related, including weight loss, postural hypotension, and dry mouth.

Other adverse reactions of potential clinical importance reported in Study 1 by 1% or more of patients treated with rasagiline 1 mg/day as adjunct to levodopa therapy, and at least as frequent as in the placebo group, in descending order of frequency include: skin carcinoma, anemia, albuminuria, amnesia, arthritis, burnitis, cerebrovascular accident, confusion, dysphagia, epistaxis, leg cramps, pruritus, skin ulcer.

There were no significant differences in the safety profile based on age or gender.

Other adverse reactions observed during all Phase 2/3 Clinical Trials:

Rasagiline was administered to approximately 1361 patients during all PD phase 2/3 clinical trials. About 283 patients received rasagiline for at least one year, approximately 410 patients received rasagiline for at least two years, 116 patients received rasagiline for at least 3 years, and 245 patients received rasagiline for more than 3 years, with some patients treated for more than 5 years. The long-term safety profile was similar to that observed with shorter duration exposure.

The frequencies listed below represent the proportion of the 1361 individuals exposed to rasagiline who experienced events of the type cited.
All events that occurred at least twice (or once for serious or potentially serious events), except those already listed above, trivial events, terms too vague to be meaningful, adverse events with no plausible relation to treatment, and events that would be expected in patients of the age studied, were reported without regard to determination of a causal relationship to rasagiline.

Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are defined as those occurring in at least 1/100 patients, infrequent adverse events are defined as those occurring in at least 1/100 to 1/1000 patients and rare adverse events are defined as those occurring in fewer than 1/1000 patients.

**Body as a whole:**
- **Frequent:** asthenia
- **Infrequent:** chills, face edema, flank pain, photosensitivity reaction

**Cardiovascular system:**
- **Frequent:** bundle branch block
- **Infrequent:** deep thrombophlebitis, heart failure, migraine, myocardial infarct, phlebitis, ventricular tachycardia
- **Rare:** arterial thrombosis, atrial arrhythmia, AV block complete, AV block second degree, bigeminy, cerebral hemorrhage, cerebral ischemia, ventricular fibrillation

**Digestive system:**
- **Frequent:** gastrointestinal hemorrhage
- **Infrequent:** colitis, esophageal ulcer, esophagitis, fecal incontinence, intestinal obstruction, mouth ulceration, stomach ulcer, stomatitis, tongue edema
- **Rare:** hematemesis, hemorrhagic gastritis, intestinal perforation, intestinal stenosis, jaundice, large intestine perforation, megalon, melena

**Hemic and Lymphatic system:**
- **Infrequent:** macrocytic anemia
- **Rare:** purpura, thrombocythemia

**Musculoskeletal system:**
- **Infrequent:** bone necrosis, muscle atrophy
- **Rare:** arthrosis

**Nervous system:**
- **Frequent:** abnormal gait, anxiety, hyperkinesia, hypertonia, neuropathy, tremor
- **Infrequent:** agitation, aphasia, circumoral paresthesia, convulsion, delusions, dementia, dysarthria, dysautonomia, dysesthesia, emotional lability, facial paralysis, foot drop, hemiplegia, hyposthesia, incoordination, manic reaction, myoclonus, neuritis, neurosis, paranoid reaction, personality disorder, psychosis, wrist drop
- **Rare:** apathy, delirium, hostility, manic depressive reaction, myelitis, neuralgia, psychotic depression, stupor

**Respiratory system:**
- **Frequent:** cough increased
- **Infrequent:** apnea, emphysema, laryngismus, pleural effusion, pneumothorax
- **Rare:** interstitial pneumonia, larynx edema, lung fibrosis

**Skin and Appendages:**
- **Infrequent:** eczema, urticaria
- **Rare:** exfoliative dermatitis, leukoderma

**Special senses:**
- **Infrequent:** blepharitis, deafness, diplopia, eye hemorrhage, eye pain, glaucoma, keratitis, ptosis, retinal degeneration, taste perversion, visual field defect
- **Rare:** blindness, parosmia, photophobia, retinal detachment, retinal hemorrhage, strabismus, taste loss, vestibular disorder

**Urogenital system:**
- **Frequent:** hematuria, urinary incontinence
- **Infrequent:** acute kidney failure, dysmenorrhea, dysuria, kidney calculus, nocturia, polyuria, scrotal edema, sexual function abnormal, urinary retention, urination impaired, vaginal hemorrhage, vaginal moniliasis, vaginitis
- **Rare:** abnormal ejaculation, amenorrhea, anuria, epididymitis, gynecomastia, hydroureter, leukorrhea, priapism

6.2 Post-marketing Experience

The following adverse events not described in sections 4 and 5 have been identified during the post-marketing/post-approval use of AZILECT. Because these adverse events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency nor to establish unequivocally a causal relationship to drug exposure: Increased libido including hypersexuality, impulse control symptoms, pathological gambling [see Patient Counseling Information (17.11)]

7 DRUG INTERACTIONS

7.1 Meperidine

Serious, sometimes fatal reactions have been precipitated with concomitant use of meperidine (e.g., Demerol and other tradenames) and MAO inhibitors including selective MAO-B inhibitors [see Contraindications (4.1)].

7.2 Dextromethorphan

The concomitant use of AZILECT and dextromethorphan was not allowed in clinical studies. The combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior. There-
fore, in view of AZILECT’s MAO inhibitory activity, dextromethorphan should not be used concomitantly with AZILECT [see Contraindications (4.2)].

7.3 Sympathomimetic Medications
The concomitant use of AZILECT and sympathomimetic medications was not allowed in clinical studies. Severe hypertensive reactions have followed the administration of sympathomimetics and non-selective MAO inhibitors. One case of hypertensive crisis has been reported in a patient taking the recommended dose of a selective MAO-B inhibitor and a sympathomimetic medication (ephrineph). Elevated blood pressure was reported in another patient taking the recommended dose of AZILECT and ophthalmic drops with a sympathomimetic medication (tetrahydrozoline).

Because AZILECT is a selective MAOI, hypertensive reactions are not ordinarily expected with the concomitant use of sympathomimetic medications. Nevertheless, caution should be exercised when concomitantly using recommended doses of AZILECT with any sympathomimetic medications including nasal, oral, and ophthalmic decongestants and cold remedies.

7.4 MAO Inhibitors
AZILECT should not be administered along with other MAO inhibitors because of the increased risk of non-selective MAO inhibition that may lead to a hypertensive crisis [see Contraindications (4.3)].

7.5 Antidepressants
Concomitant use of AZILECT with one of many classes of antidepressants (e.g., SSRIs, SNRIs, triazolopyridine, tricyclic or tetracyclic antidepressants) is not recommended [see Warnings and Precautions (5.1)].

7.6 Levodopa/Carbidopa
[see Warnings and Precautions (5.6) and Clinical Pharmacology (12.3)].

7.7 Ciprofloxacin and Other CYP1A2 Inhibitors
Rasagiline plasma concentrations may increase up to 2 fold in patients using concomitant ciprofloxacin and other CYP1A2 inhibitors. This could result in increased adverse events [see Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)].

7.8 Theophylline
[see Clinical Pharmacology (12.3)].

7.9 Tyramine/Rasagiline Interaction
MAO in the gastrointestinal tract and liver (primarily type A) is thought to provide vital protection from exogenous amines (e.g., tyramine) that have the capacity, if absorbed intact, to cause a “hypertensive crisis,” the so-called “cheese reaction”. If large amounts of certain exogenous amines (e.g., from fermented cheese, herring, over-the-counter cough/cold medications) gain access to the systemic circulation because MAO-A has been inhibited, they cause release of norepinephrine which may result in a rise in systemic blood pressure. MAOIs that selectively inhibit MAO-B are largely devoid of the potential to cause tyramine-induced hypertensive crisis.

Results of a special tyramine challenge study indicate that rasagiline is selective for MAO-B at recommended doses and can ordinarily be used without dietary tyramine restriction. However, certain foods (e.g., aged cheeses, such as Stilton cheese) may contain very high amounts (i.e., > 150 mg) of tyramine and could potentially cause a hypertensive cheese reaction in patients taking AZILECT due to mild increased sensitivity to tyramine. Patients should be advised to avoid foods (e.g., aged cheese) containing a very large amount of tyramine while taking recommended doses of AZILECT because of the potential for large increases in blood pressure. Selectivity for inhibiting MAO-B diminishes in a dose-related manner as the dose is progressively increased above the recommended daily doses.

There were no cases of hypertensive crisis in the clinical development program associated with 1 mg daily rasagiline treatment, in which most patients did not follow dietary tyramine restriction.

Despite the selective inhibition of MAO-B at recommended doses of AZILECT, there have been post-marketing reports of patients who experienced significantly elevated blood pressure (including rare cases of hypertensive crisis) after ingestion of unknown amounts of tyramine-rich foods while taking recommended doses of AZILECT [see Dosing and Administration (2), and Warnings and Precautions (5.4)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Category C

No effect on embryo-fetal development was observed in a combined mating/fertility and embryo-fetal development study in female rats at doses up to 3 mg/kg/day (approximately 30 times the expected plasma rasagiline exposure [AUC] at the maximum recommended human dose [MRHD, 1 mg/day]). Effects on embryo-fetal development in rabbit have not been adequately assessed.

In a study in which pregnant rats were dosed with rasagiline (0.1, 0.3, 1 mg/kg/day) orally, from the beginning of organogenesis to day 20 post-partum, offspring survival was decreased and offspring body weight was reduced at doses of 0.3 mg/kg/day and 1 mg/kg/day (10 and 16 times the expected plasma rasagiline exposure [AUC] at the MRHD). No plasma data were available at the no-effect dose (0.1 mg/kg); however, that dose is 1 times the MRHD on a mg/m^2 basis. Rasagiline’s effect on physical and behavioral development was not adequately assessed in this study.

Rasagiline may be given as an adjunct therapy to levodopa/carbidopa treatment. In a study in which pregnant rats were dosed with rasagiline (0.1, 0.3, 1 mg/kg/day) and levodopa/carbidopa (80/20 mg/kg/day) alone and in combination throughout the period of organogenesis, there was an increased incidence of wavy ribs in fetuses from rats treated with rasagiline in combination with levodopa/carbidopa at 1/80/20 mg/kg/day (approximately 8 times the plasma AUC expected in humans at the MRHD and 1/4 times the MRHD of levodopa/carbidopa [800/200 mg/day] on a mg/m^2 basis). In a study in which pregnant rabbits were dosed throughout the period of organogenesis with rasagiline alone (3 mg/kg) or in combination with levodopa/carbidopa (rasagiline: 0.1, 0.6, 1.2 mg/kg, levodopa/carbidopa: 80/20 mg/kg/day), an increase in embryo-fetal death was noted at rasagiline doses of 0.6 and 1.2 mg/kg/day when administered in combination with levodopa/carbidopa (approximately 7 and 13 times, respectively, the plasma rasagiline AUC at the MRHD). There was an increase in cardiovascular abnormalities with levodopa/carbidopa alone (1/1 times the MRHD on a mg/m^2 basis) and to a greater extent when rasagiline (at all doses; 1-13 times the plasma rasagiline AUC at the MRHD) was administered in combination with levodopa/carbidopa.
There are no adequate and well-controlled studies of rasagiline in pregnant women. Therefore, AZILECT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers
In rats rasagiline was shown to inhibit prolactin secretion and it may inhibit milk secretion in females.

It is not known whether rasagiline is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when AZILECT is administered to a nursing woman.

8.4 Pediatric Use
The safety and effectiveness of AZILECT in the pediatric population have not been studied.

8.5 Geriatric Use
Approximately half of patients in clinical trials were 65 years and over. There were no significant differences in the safety profile of the geriatric and non-geriatric patients.

8.6 Hepatic Impairment
Rasagiline plasma concentration may be increased in patients with mild (up to 2 fold, Child-Pugh score 5-6), moderate (up to 7 fold, Child-Pugh score 7-9), and severe (Child-Pugh score 10-15) hepatic impairment. Patients with mild hepatic impairment should be given a dose of 0.5 mg/day. AZILECT should not be used in patients with moderate or severe hepatic impairment. (see Dosage and Administration (2.3), Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)).

8.7 Renal Impairment
Dose adjustment of AZILECT is not required for patients with mild or moderate renal impairment because AZILECT plasma concentrations are not increased in patients with moderate renal impairment. Rasagiline has not been studied in patients with severe renal impairment.

9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
AZILECT is not a controlled substance.

9.2 Abuse
Studies conducted in mice and rats did not reveal any potential for drug abuse and dependence. Clinical trials have not revealed any evidence of the potential for abuse, tolerance or physical dependence; however, systematic studies in humans designed to evaluate these effects have not been performed.

9.3 Dependence
Studies conducted in mice and rats did not reveal any potential for drug abuse and dependence. Clinical trials have not revealed any evidence of the potential for abuse, tolerance or physical dependence; however, systematic studies in humans designed to evaluate these effects have not been performed.

10 OVERDOSE
No cases of AZILECT overdose were reported in clinical trials.

Rasagiline was well tolerated in a single-dose study in healthy volunteers receiving 20 mg/day and in a ten-day study in healthy volunteers receiving 10 mg/day. Adverse events were mild or moderate. In a dose escalation study in patients on chronic levodopa therapy treated with 10 mg of rasagiline there were three reports of cardiovascular side effects (including hypertension and postural hypotension) which resolved following treatment discontinuation.

Symptoms of overdosage, although not observed with rasagiline during clinical development, may resemble those observed with non-selective MAO inhibitors (MAOIs).

Although no cases of overdose have been observed with rasagiline during the clinical development program, the following description of presenting symptoms and clinical course is based upon overdose descriptions of non-selective MAO inhibitors. Characteristically, signs and symptoms of non-selective MAOI overdose may not appear immediately. Delays of up to 12 hours between ingestion of drug and the appearance of signs may occur. Importantly, the peak intensity of the syndrome may not be reached for upwards of a day following the overdose. Death has been reported following overdosage. Therefore, immediate hospitalization, with continuous patient observation and monitoring for a period of at least two days following the ingestion of such drugs in overdose, is strongly recommended.

The clinical picture of MAOI overdose varies considerably; its severity may be a function of the amount of drug consumed. The central nervous and cardiovascular systems are prominently involved.

Signs and symptoms of overdosage may include, alone or in combination, any of the following: drowsiness, dizziness, faintness, irritability, hyperactivity, agitation, severe headache, hallucinations, trismus, opisthotonos, convulsions, and coma; rapid and irregular pulse, hypertension, hypotension and vascular collapse; precordial pain, respiratory depression and failure, hyperpyrexia, diaphoresis, and cool, clammy skin.

There is no specific antidote for rasagiline overdose. The following suggestions are offered based upon the assumption that rasagiline overdose may be modeled after non-selective MAO inhibitor poisoning. Treatment of overdose with non-selective MAO inhibitors is symptomatic and supportive. Respiration should be supported by appropriate measures, including management of the airway, use of supplemental oxygen, and mechanical ventilatory assistance, as required. Body temperature should be monitored closely. Intensive management of hyperpyrexia may be required. Maintenance of fluid and electrolyte balance is essential. For this reason, in cases of overdose with AZILECT, dietary tyramine restriction should be observed for several weeks to avoid the risk of a hypertensive/cheese reaction.

A poison control center should be called for the most current treatment guidelines.

A post-marketing report described a single patient who developed a non-fatal serotonin syndrome after ingesting 100 mg of AZILECT in a suicide attempt. Another patient who was treated in error with 4 mg AZILECT daily and tramadol also developed a serotonin syndrome. One patient who was treated in error with 3 mg AZILECT daily experienced alternating episodes of vascular fluctuations consisting of hypertension and orthostatic hypotension.

11 DESCRIPTION
AZILECT® tablets contain rasagiline (as the mesylate), a propargylamine-based drug indicated for the treatment of idiopathic Parkinson’s disease. It is designated chemically as: 1H-Inden-1-amine, 2, 3-dihydro-N-2-propynyl- (1R)-, methanesulfonate. The empirical formula of rasagiline mesylate is (C12H13N)CH4SO3 and its molecular weight is 267.34.
Rasagiline mesylate is a white to off-white powder, freely soluble in water or ethanol and sparingly soluble in isopropanol. Each AZILECT tablet for oral administration contains rasagiline mesylate equivalent to 0.5 mg or 1 mg of rasagiline base. Each AZILECT tablet also contains the following inactive ingredients: mannitol, starch, pregelatinized starch, colloidal silicon dioxide, stearic acid and talc.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

AZILECT functions as a selective, irreversible MAO-B inhibitor indicated for the treatment of idiopathic Parkinson's disease. The results of a clinical trial designed to examine the effects of Azilect on blood pressure when it is administered with increasing doses of tyramine indicates the functional selectivity can be incomplete when healthy subjects ingest large amounts of tyramine while receiving recommended doses of AZILECT. The selectivity for inhibiting MAO-B diminishes in a dose-related manner.

MAO, a flavin-containing enzyme, is classified into two major molecular species, A and B, and is localized in mitochondrial membranes throughout the body in nerve terminals, brain, liver and intestinal mucosa. MAO regulates the metabolic degradation of catecholamines and serotonin in the CNS and peripheral tissues. MAO-B is the major form in the human brain. In ex vivo animal studies in brain, liver and intestinal tissues, rasagiline was shown to be a potent, irreversible monoamine oxidase type B (MAO-B) selective inhibitor. Rasagiline at the recommended therapeutic dose was also shown to be a potent and irreversible inhibitor of MAO-B in platelets. The precise mechanisms of action of rasagiline are unknown. One mechanism is believed to be related to its MAO-B inhibitory activity, which causes an increase in extracellular levels of dopamine in the striatum. The elevated dopamine level and subsequent increased dopaminergic activity are likely to mediate rasagiline’s beneficial effects seen in models of dopaminergic motor dysfunction.

12.2 Pharmacodynamics

Platelet MAO Activity in Clinical Studies

Studies in healthy subjects and in Parkinson's disease patients have shown that rasagiline inhibits platelet MAO-B irreversibly. The inhibition lasts at least 1 week after last dose. Almost 25-35% MAO-B inhibition was achieved after a single rasagiline dose of 1 mg/day and more than 55% of MAO-B inhibition was achieved after a single rasagiline dose of 2 mg/day. Over 90% inhibition was achieved 3 days after rasagiline daily dosing at 2 mg/day and this inhibition level was maintained 3 days post-dose. Multiple doses of rasagiline of 0.5, 1 and 2 mg per day resulted in complete MAO-B inhibition.

12.3 Pharmacokinetics

Rasagiline in the range of 1-6 mg demonstrated a more than proportional increase in AUC, while Cmax was dose proportional. Rasagiline mean steady-state half life is 3 hours but there is no correlation of pharmacokinetics with its pharmacological effect because of its irreversible inhibition of MAO-B.

Absorption

Rasagiline is rapidly absorbed, reaching peak plasma concentration (Cmax) in approximately 1 hour. The absolute bioavailability of rasagiline is about 36%. Food does not affect the Tmax of rasagiline, although Cmax and exposure (AUC) are decreased by approximately 60% and 20%, respectively, when the drug is taken with a high fat meal. Because AUC is not significantly affected, AZILECT can be administered with or without food (see Dosage and Administration (2)).

Distribution

The mean volume of distribution at steady-state is 87 L, indicating that the tissue binding of rasagiline is in excess of plasma protein binding. Plasma protein binding ranges from 88-94% with mean extent of binding of 61-63% to human albumin over the concentration range of 1-100 ng/mL.

Metabolism and Elimination

Rasagiline undergoes almost complete biotransformation in the liver prior to excretion. The metabolism of rasagiline proceeds through two main pathways: N-dealkylation and/or hydroxylation to yield 1-aminoindan (AI), 3-hydroxy-N-propargyl-1 aminoindan (3-OH-PAI) and 3-hydroxy-1-aminoindan (3-OH-AI). In vitro experiments indicate that both routes of rasagiline metabolism are dependent on the cytochrome P450 (CYP) system, with CYP1A2 being the major isoenzyme involved in rasagiline metabolism. Glucuronide conjugation of rasagiline and its metabolites, with subsequent excretion, is the major elimination pathway.

After oral administration of 14C-labeled rasagiline, elimination occurred primarily via urine and secondarily via feces (62% of total dose in urine and 7% of total dose in feces over 7 days), with a total calculated recovery of 84% of the dose over a period of 38 days. Less than 1% of rasagiline was excreted as unchanged drug in urine.

Special Populations

Hepatic Impairment

Following repeat dose administration (7 days) of rasagiline (1 mg/day) in subjects with mild hepatic impairment (Child-Pugh score 5-6), AUC and Cmax were increased by 2 fold and 1.4 fold, respectively, compared to healthy subjects. In subjects with moderate hepatic impairment (Child-Pugh score 7-9), AUC and Cmax were increased by 7 fold and 2 fold, respectively, compared to healthy subjects (see Dosage and Administration (2.3) and Warnings and Precautions (5.3)).

Renal Impairment

Following repeat dose administration (8 days) of rasagiline (1 mg/day) in subjects with moderate renal impairment, rasagiline exposure (AUC) was similar to rasagiline exposure in healthy subjects, while the major metabolite 1-Al exposure (AUC) was increased 1.5-fold in subjects with moderate renal impairment, compared to healthy subjects. Because...
1-A1 is not an MAO inhibitor, no dose adjustment is needed for patients with mild and moderate renal impairment. Data are not available for patients with severe renal impairment.

**Elderly**
Since age has little influence on rasagiline pharmacokinetics, it can be administered at the recommended dose in the elderly (≥65 years).

**Pediatric**
AZILECT has not been investigated in patients below 18 years of age.

**Gender**
The pharmacokinetic profile of rasagiline is similar in men and women.

**Drug-Drug Interactions**

**Tyramine Effect**
[see Dosage and Administration (2), Warnings and Precautions (5.4), and Drug Interactions (7.9)].

**Levodopa**
Data from population pharmacokinetic studies comparing rasagiline clearance in the presence and absence of levodopa have given conflicting results. Although there may be some increase in rasagiline blood levels in the presence of levodopa, the effect is modest and rasagiline dosing need not be modified in the presence of levodopa.

**Effect of Other Drugs on the Metabolism of AZILECT**

In vitro metabolism studies showed that CYP1A2 was the major enzyme responsible for the metabolism of rasagiline. There is the potential for inhibitors of this enzyme to alter AZILECT clearance when coadministered [see Dosage and Administration (2.5) and Warnings and Precautions (5.2)].

**Ciprofloxacin:** When ciprofloxacin, an inhibitor of CYP1A2, was administered to healthy volunteers (n=12) at 500 mg (BI) with rasagiline at 2 mg/day, the AUC of rasagiline increased by 83% and there was no change in the elimination half life [see Dosage and Administration (2.5) and Warnings and Precautions (5.2)].

**Theophylline:** Coadministration of rasagiline 1 mg/day and theophylline, a substrate of CYP1A2, up to 500 mg twice daily to healthy subjects (n=24) did not affect the pharmacokinetics of either drug.

**Antidepressants:** Severe CNS toxicity (occasionally fatal) associated with hyperpyrexia as part of a serotonin syndrome, has been reported with combined treatment of an antidepressant (e.g., from one of many classes including tricyclic or tetracyclic antidepressants, SSRIs, SNRIs, triazolopyridine antidepressants) and non-selective MAO-B inhibitor [see Warnings and Precautions (5.1)].

**Effect of AZILECT on Other Drugs**
No additional in vivo trials have investigated the effect of AZILECT on other drugs metabolized by the cytochrome P450 enzyme system. In vitro studies showed that rasagiline at a concentration of 1mcg/ml (equivalent to a level that is 160 times the average Cmax – 5.9-8.5 ng/mL in Parkinson’s disease patients after 1 mg rasagiline multiple dosing) did not inhibit cytochrome P450 isoenzymes, CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4 and CYP4A. These results indicate that rasagiline is unlikely to cause any clinically significant interference with substrates of these enzymes.

13 Nonclinical Toxicology

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

**Carcinogenesis**
Two year carcinogenicity studies were conducted in CD-1 mice at oral (gavage) doses of 1, 15, and 45 mg/kg and in Sprague-Dawley rats at oral (gavage) doses of 0.3, 1, and 3 mg/kg (males) or 0.5, 2, 5, and 17 mg/kg (females). In rats, there was no increase in tumors at any dose tested. Plasma exposures at the highest dose tested were approximately 33 and 260 times, in male and female rats, respectively, the expected plasma exposures in humans at the maximum recommended dose (MRD) of 1 mg/day.

In mice, there was an increase in lung tumors (combined adenomas/carcinomas) at 15 and 45 mg/kg males and females. Plasma exposures associated with the no-effect dose (1 mg/kg) were approximately 5 times those expected in humans at the MRD.

The carcinogenic potential of rasagiline administered in combination with levodopa/carbidopa has not been examined.

**Mutagenesis**
Rasagiline was reproducibly clastogenic in in vitro chromosomal aberration assays in human lymphocytes in the presence of metabolic activation and was mutagenic and clastogenic in the in vitro mouse lymphoma tk assay in the absence and presence of metabolic activation. Rasagiline was negative in the in vitro bacterial reverse mutation (Ames) assay, the in vivo unscheduled DNA synthesis assay, and the in vivo micronucleus assay in CD-1 mice. Rasagiline was also negative in the in vivo micronucleus assay in CD-1 mice when administered in combination with levodopa/carbidopa.

**Impairment of Fertility**
Rasagiline had no effect on mating performance or fertility in male rats treated prior to and throughout the mating period, or in female rats treated from prior to mating through day 17 of gestation at oral doses up to 3 mg/kg/day (approximately 30 times the expected plasma rasagiline exposure (AUC) at the maximum recommended human dose [1 mg/day]). The effect of rasagiline administered in combination with levodopa/carbidopa on mating and fertility has not been examined.

14 CLINICAL TRIALS

The effectiveness of AZILECT for the treatment of Parkinson’s disease was established in three 18- to 26-week, randomized, placebo-controlled trials. In one of these trials AZILECT was given as initial monotherapy and in the other two as adjunctive therapy to levodopa.

14.1 Monotherapy Use of AZILECT
The monotherapy trial was a double-blind, randomized, fixed-dose parallel group, 26-week study in early Parkinson’s disease patients not receiving any concomitant dopaminergic therapy at the start of the study. The majority of the patients were not treated with any anti-Parkinson’s disease medication before receiving rasagiline treatment.

In this trial, 404 patients were randomly assigned to receive placebo (138 patients), rasagiline 1 mg/day (134 patients) or rasagiline 2 mg/day (132 patients). Patients were not allowed to take levodopa, dopamine agonists, selegiline or...
amantadine, but if necessary, could take stable doses of anticholinergic medication. The average Parkinson’s disease duration was approximately 1 year (range 0 to 11 years).

The primary measure of effectiveness was the change from baseline in the total score of the Unified Parkinson’s Disease Rating Scale (UPDRS), (mentation (Part I) + activities of daily living (ADL) (Part II) + motor function (Part III)). The UPDRS is a multi-item rating scale that measures the ability of a patient to perform mental and motor tasks as well as activities of daily living. A reduction in the score represents improvement and a beneficial change from baseline appears as a negative number.

Rasagiline (1 or 2 mg once daily) had a significant beneficial effect relative to placebo on the primary measure of effectiveness in patients receiving six months of treatment and not on dopaminergic therapy. Patients who received rasagiline had significantly less worsening in the UPDRS score, compared to those who received placebo. The effectiveness of rasagiline 1 mg and 2 mg was comparable. Table 3 displays the results of the monotherapy trial.

### Table 3. Parkinson’s Disease Patients not on Dopaminergic Therapy (Monotherapy)

<table>
<thead>
<tr>
<th>Primary Measure of Effectiveness: Change in total UPDRS score</th>
<th>Baseline score</th>
<th>Change from baseline to termination score</th>
<th>p-value vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>24.5</td>
<td>3.9</td>
<td>---</td>
</tr>
<tr>
<td>1.0 mg/day</td>
<td>24.7</td>
<td>0.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>2.0 mg/day</td>
<td>25.9</td>
<td>0.7</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

For the comparison between rasagiline 1 mg/day and placebo, no differences in effectiveness based on age or gender were detected.

### 14.2 Adjunctive Use of AZILECT

Two multicenter, randomized, multinational trials were conducted in more advanced Parkinson’s disease patients treated chronically with levodopa and experiencing motor fluctuations (including but not limited to, end of dose “wearing off,” sudden or random “off,” etc.). The first (Study 1) was conducted in North America (U.S. and Canada) and compared two doses (0.5 mg and 1 mg daily) of rasagiline and placebo while the second (Study 2) was conducted outside of North America (several European countries, Argentina, Israel) and studied only a single dose (1 mg daily) of rasagiline and placebo. Patients had had Parkinson’s disease for an average of 9 years (range 5 months to 33 years), had been taking levodopa for an average of 8 years (range 5 months to 32 years), and had been experiencing motor fluctuations for approximately 3 to 4 years (range 1 month to 23 years). Patients kept home diaries just prior to baseline and at specified intervals during the trial. Diaries recorded one of the following four conditions for each half-hour interval over a 24-hour period: “ON” (period of relatively good function and mobility) as either “ON” with no dyskinesia or without troublesome dyskinesia, or “OFF” with troublesome dyskinesia, “OFF” (period of relatively poor function and mobility) or asleep. “Troublesome” dyskinesia is defined as that which interferes with the patient’s daily activity. All patients had been inadequately controlled and were experiencing motor fluctuations typical of advanced stage disease despite receiving levodopa/decarboxylase inhibitor. The average dose of levodopa/decarboxylase inhibitor was approximately 700 to 800 mg (range 150 to 3000 mg/day). Patients were also allowed to take stable doses of additional anti-PD medications at entry into the trials. In both trials, approximately 65% of patients were on dopamine agonists and in the North American study (Study 1) approximately 35% were on entacapone. The majority of patients taking entacapone were taking a dopamine agonist as well.

In both trials the primary measure of effectiveness was the change in the mean number of hours that were spent in the “OFF” state at baseline compared to the mean number of hours that were spent in the “OFF” state during the treatment period. The first adjunct study (Study 1) was a double-blind, randomized, fixed-dose, parallel group trial conducted in 472 levodopa-treated Parkinson’s disease patients who were experiencing motor fluctuations. Patients were randomly assigned to receive placebo (159 patients), rasagiline 0.5 mg/day (164 patients), or rasagiline 1 mg/day (149 patients), and were treated for 26 weeks. Patients averaged approximately 6 hours daily in the “OFF” state at baseline, as confirmed by home diaries.

The second adjunct study (Study 2) was a double-blind, randomized, parallel group trial conducted in 687 levodopa-treated Parkinson’s disease patients who were experiencing motor fluctuations. Patients were randomly assigned to receive placebo (229 patients), rasagiline 1 mg/day (231 patients) or an active comparator, a COMT inhibitor taken along with scheduled doses of levodopa/decarboxylase inhibitor (227 patients). Patients were treated for 18 weeks. Patients averaged approximately 5.6 hours daily in the “OFF” state at baseline as confirmed by home diaries.

In both studies, rasagiline 1 mg once daily reduced “OFF” time compared to placebo when added to levodopa in patients experiencing motor fluctuations (Tables 4 and 5). The lower dose (0.5 mg) of rasagiline also significantly reduced “OFF” time (Table 4), but had a numerically smaller effect than the 1 mg dose of rasagiline. In Study 2, the active comparator also reduced “OFF” time when compared to placebo.

### Table 4. Parkinson’s Disease Patients Receiving AZILECT as Adjunct Therapy (Study 1)

<table>
<thead>
<tr>
<th>Primary Measure of Effectiveness: Change in mean total daily “OFF” time</th>
<th>Baseline (hours)</th>
<th>Change from baseline to treatment period (hours)</th>
<th>p-value vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>6.0</td>
<td>-0.9</td>
<td>---</td>
</tr>
<tr>
<td>0.5 mg/day</td>
<td>6.0</td>
<td>-1.4</td>
<td>0.0199</td>
</tr>
<tr>
<td>1.0 mg/day</td>
<td>6.3</td>
<td>-1.9</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
In both studies, dosage reduction of levodopa was allowed within the first 6 weeks if dopaminergic side effects, including dyskinesia and hallucinations, emerged. In Study 1, levodopa dosage reduction occurred in 8% of patients in the placebo group and in 16% and 17% of patients in the 0.5 mg/day and 1 mg/day rasagiline groups, respectively. In those patients who had levodopa dosage reduced, the dose was reduced on average by about 7%, 9%, and 13% in the placebo, 0.5 mg/day, and 1 mg/day groups, respectively. In Study 2, levodopa dosage reduction occurred in 6% of patients in the placebo group and in 9% in the rasagiline 1 mg/day group. In patients who had their levodopa dosage reduced, the dose was reduced on average by about 13% and 11% in the placebo and the rasagiline groups, respectively.

For the comparison between rasagiline 1 mg/day and placebo in both studies, no differences in effectiveness based on age or gender were detected.

Several secondary outcome assessments in the two studies showed statistically significant improvements with rasagiline. These included effects on the activities of daily living (ADL) subscale of the UPDRS performed during an “OFF” period and the motor subscale of the UPDRS performed during an “ON” period. In both scales, a negative response represents improvement. Tables 6 and 7 show these results for Studies 1 and 2.

### Table 6. Secondary Measures of Effectiveness (Study 1)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (score)</th>
<th>Change from baseline to last value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UPDRS ADL (Activities of Daily Living) subscale score while “OFF”</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>15.5</td>
<td>0.68</td>
</tr>
<tr>
<td>0.5 mg/day</td>
<td>15.8</td>
<td>-0.60</td>
</tr>
<tr>
<td>1.0 mg/day</td>
<td>15.5</td>
<td>-0.68</td>
</tr>
<tr>
<td><strong>UPDRS Motor subscale score while “ON”</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>20.8</td>
<td>1.21</td>
</tr>
<tr>
<td>0.5 mg/day</td>
<td>21.5</td>
<td>-1.43</td>
</tr>
<tr>
<td>1.0 mg/day</td>
<td>20.9</td>
<td>-1.30</td>
</tr>
</tbody>
</table>

### Table 7. Secondary Measures of Effectiveness (Study 2)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (score)</th>
<th>Change from baseline to last value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UPDRS ADL (Activities of Daily Living) subscale score while “OFF”</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>18.7</td>
<td>-0.89</td>
</tr>
<tr>
<td>1.0 mg/day</td>
<td>19.0</td>
<td>-2.61</td>
</tr>
<tr>
<td><strong>UPDRS Motor subscale score while “ON”</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>23.5</td>
<td>-0.82</td>
</tr>
<tr>
<td>1.0 mg/day</td>
<td>23.8</td>
<td>-3.87</td>
</tr>
</tbody>
</table>

16 **HOW SUPPLIED**
AZILECT 0.5 mg Tablets:
White to off-white, round, flat, beveled tablets, debossed with “GIL 0.5” on one side and plain on the other side. Supplied as bottles of 30 tablets (NDC 68546-142-56).
AZILECT 1 mg Tablets:
White to off-white, round, flat, beveled tablets, debossed with “GIL 1” on one side and plain on the other side. Supplied as bottles of 30 tablets (NDC 68546-229-56).
Storage:
Store at 25°C (77°F) with excursions permitted to 15°C-30°C (59°F-86°F).

17 **INFORMATION FOR PATIENTS**
17.1 Coadministration of Antidepressants and Other Drugs
Patients should inform their physician if they are taking, or planning to take, any prescription or over-the-counter drugs, especially antidepressants and over-the-counter cold medications, since there is a potential for interaction with AZILECT. Because patients should not use meperidine or certain other analgesics with AZILECT, they should contact their healthcare provider before taking analgesics [see Warnings and Precautions (5.1)].
17.2 Ciprofloxacin or Other CYP1A2 Inhibitors
Patients should be informed that they should contact their healthcare provider of AZILECT if they take ciprofloxacin or a similar drug that could increase blood levels of rasagiline because of the need to adjust the dose of AZILECT [see Warnings and Precautions (5.2)].

17.3 Risk of Hypertensive Crisis and Nonselective Monoamine Oxidase Inhibition Above the Recommended Doses
Patients should be advised not to exceed the maximum recommended daily dose of 1 mg/day (0.5 mg/day for subjects with mild hepatic impairment and subjects using concomitant ciprofloxacin and other CYP1A2 inhibitors).

The risk of using higher than recommended daily doses of AZILECT should be explained, and a brief description of the hypertensive/cheese reaction provided.

The possibility exists that very tyramine-rich foods (e.g., aged cheese such as Stilton) could possibly cause an increase in blood pressure. Patients should be advised to avoid certain foods (e.g., aged cheese) containing a very large amount of tyramine while taking recommended doses of AZILECT because of the potential for large increases in blood pressure. If patients eat foods very rich in tyramine and do not feel well soon after eating, they should contact their healthcare provider [see Warnings and Precautions (5.4)].

17.4 Melanoma
It is not known if melanoma is associated with Parkinson’s disease or the medicines used to treat Parkinson’s disease. Patients being treated with AZILECT should be advised to have periodic skin examinations. [see Warnings and Precautions (5.5)].

17.5 Dyskinesia
Patients taking AZILECT as adjunct to levodopa should be advised that there is a possibility of dyskinesia or increased dyskinesia [see Warnings and Precautions (5.6)].

17.6 Lowering of Blood Pressure and Postural/Orthostatic Hypotension
Patients should be advised that they may develop postural (orthostatic) hypotension with or without symptoms such as dizziness, nausea, syncope, and sometimes sweating. Hypotension and/or orthostatic symptoms may occur more frequently during initial therapy or with an increase in dose at any time (cases have been seen after weeks of treatment). Accordingly, patients should be cautioned against standing up rapidly after sitting or lying down, especially if they have been doing so for prolonged periods, and especially, at the initiation of treatment with AZILECT [see Warnings and Precautions (5.7)].

17.7 Elevation of Blood Pressure
Patients should be alerted to the possibility of increases in blood pressure during treatment with AZILECT. Exacerbation of hypertension may occur. Medication dose adjustment may be necessary if elevation of blood pressure is sustained over multiple evaluations [see Warnings and Precautions (5.8)].

17.8 Hallucinations/Psychotic-Like Behavior
Patients should be informed that hallucinations or other manifestations of psychotic-like behavior can occur when taking AZILECT. Patients should also be advised that, if they have a major psychotic disorder, that AZILECT should not ordinarily be used because of the risk of exacerbating the psychosis. Patients with a major psychotic disorder should also be aware that many treatments for psychosis may decrease the effectiveness of AZILECT [see Warnings and Precautions (5.9)].

17.9 Withdrawal-Emergent Hyperpyrexia and Confusion
Patients should be told to contact their healthcare provider if they wish to discontinue Azilect.

17.10 Missing Dose
Patients should be instructed to take AZILECT as prescribed. If a dose is missed, the patient should not double-up the dose of AZILECT. The next dose should be taken at the usual time on the following day.

17.11 Impulse Control/Compulsive Behaviors
There have been reports of patients experiencing intense urges to gamble, increased sexual urges, or other intense urges, and the inability to control these urges while taking one or more of the medications that increase central dopaminergic tone and that are generally used for the treatment of Parkinson’s disease (including AZILECT). Although it is not proven that the medications caused these events, these urges were reported to have stopped in some cases when the dose was reduced or the medication was stopped. Prescribers should ask patients about the development of new or increased gambling urges, sexual urges, or other urges while being treated with rasagiline. Patients should inform their physician if they experience new or increased gambling urges, increased sexual urges, or other intense urges while taking rasagiline. Physicians should consider dose reduction or stopping the medication if a patient develops such urges while taking rasagiline.

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