Parkinson’s disease: diagnosis and management in primary and secondary care.

NICE guideline

First draft for consultation, August 2005

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.
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Introduction

Parkinson’s disease (PD) is a progressive neurodegenerative condition leading to the death of the dopamine containing cells of the substantia nigra. There is no consistently reliable test that can distinguish PD from other conditions with similar clinical presentations. The diagnosis is primarily a clinical one based on a history and examination.

People with PD classically present with the symptoms and signs associated with parkinsonism, namely bradykinesia, rigidity and rest tremor.

Less common conditions than PD also cause parkinsonism, including: multiple cerebral infarction, drugs and degenerative conditions such as progressive supra-nuclear palsy (PSP) and multiple system atrophy (MSA).

Although PD is predominantly a movement disorder, other impairments frequently develop, including psychiatric problems such as depression and dementia. Autonomic disturbances and pain (which rarely is a presenting feature of PD) may later ensue, and the condition progresses to cause significant disability and handicap with impaired quality of life for the affected individual, and indirectly for family and carers.

Health and resource implications

PD is a common, chronic, progressive neurological condition, estimated to affect 100–180 per 100,000 of the population (between 6 and 11 people per 6000 of the general population in the UK)¹ and has an annual incidence of 4–20 per 100,000. There is a rising prevalence with age and no sex differences in the prevalence of PD.

¹The size of the average general practice list in the UK.
Patient-centred care

This guideline offers best practice advice on the care of people with Parkinson’s disease.

Treatment and care should take into account patients’ individual needs and preferences. People with Parkinson’s disease should have the opportunity to make informed decisions about their care and treatment. Where patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – *Reference guide to consent for examination or treatment* (2001) (available from www.dh.gov.uk).

Good communication between healthcare professionals and patients is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.

Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in decisions about the patient’s care and treatment.

Carers and relatives should also be provided with the information and support they need.
Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

- Before treatment is initiated, people with suspected Parkinson's disease should be referred quickly\(^2\) to a specialist with expertise in the differential diagnosis of this condition. [1.2.2.1]

- The diagnosis of Parkinson's disease should be kept under regular review\(^3\) and reconsidered if atypical features develop. [1.2.3.1]

- All people with Parkinson's disease should have regular access to specialist nursing care to provide monitoring and altering of medication, a point of contact for support including home visits, and a reliable source of information about clinical and social matters relevant to Parkinson's disease. [1.7.1.1]

- At diagnosis and regular review meetings, consideration should be given to referring people with Parkinson's disease for physiotherapy, occupational therapy and speech and language therapy interventions. [1.7.2.1; 1.7.3.1; 1.7.4.1]

- NB; A recommendation on the use of cholinesterase inhibitors for dementia in PD will be made in the second consultation draft of this guideline following an analysis of their cost effectiveness. This additional work is being undertaken at the request of the National Institute for Health and Clinical Excellence [See 1.6.3.1]

\(^2\)In suspected mild Parkinson's disease people should be seen within 6 weeks but new referrals in later disease with more complex problems require an appointment within 2 weeks.

\(^3\)At 6 to 12 month intervals.
The following guidance is evidence based. Appendix A shows the grading scheme used for the recommendations: A, B, C, D or good practice point – D (GPP). Recommendations on diagnostic test are graded A (DS), B (DS), C (DS) or D (DS). A summary of the evidence on which the guidance is based is provided in the full guideline (see Section 5).

1 Guidance

1.1 Communication with people with PD

1.1.1 Communication

1.1.1.1 Communication with people with PD should empower them to participate in the judgments and choices about their own care. [D]

1.1.1.2 Discussions should achieve a balance between the provision of honest realistic information about the condition and the promotion of a feeling of optimism. [D]

1.1.1.3 As people with PD may develop impaired cognitive ability and depression, they require: [D(GPP)]

- both oral and written communication throughout the course of the disease, which should be individually tailored and reinforced as necessary
- consistent communication from the professionals involved.

1.1.1.4 Families and carers should be given information about the condition, their entitlements to care assessment and the support services available. [D (GPP)]

1.2 Diagnosing PD

1.2.1 Clinical versus post-mortem diagnosis

1.2.1.1 PD should be diagnosed clinically and based on the United Kingdom Parkinson's Disease Society Brain Bank Criteria. [B (DS)]
1.2.2 **Expert versus non-expert diagnosis**

1.2.2.1 People with suspected PD should be referred quickly\(^4\) and untreated to a specialist with expertise in the differential diagnosis of this condition. [B (DS)]

1.2.3 **Review of diagnosis**

1.2.3.1 The diagnosis of PD should be kept under regular review\(^5\) and reconsidered if atypical clinical features develop. [D (DS)]

1.2.4 **Single Photon Emission Computed Tomography (SPECT)**

1.2.4.1 \(^{123}\)I-FP-CIT SPECT should be available to specialists with expertise in the differential diagnosis of tremor. [D (DS)]

1.2.4.2 \(^{123}\)I-FP-CIT SPECT should be considered in people with tremor where essential tremor cannot be differentiated from parkinsonism. [A (DS)]

1.2.5 **Positron Emission Tomography (PET)**

1.2.5.1 PET should not be used in the differential diagnosis of parkinsonian syndromes except in the context of clinical trials. [B (DS)]

1.2.6 **Magnetic Resonance Imaging (MRI)**

1.2.6.1 Structural MRI should not be used in the diagnosis of Parkinson’s disease. [B (DS)]

1.2.6.2 Structural MRI may be useful in the differential diagnosis of parkinsonian syndromes. [D (DS)]

\(^4\) The Guideline Development Group considered that people with suspected mild PD should be seen within 6 weeks but new referrals in later disease with more complex problems require an appointment within 2 weeks.

\(^5\) The Guideline Development Group considered that people diagnosed with PD should be seen at regular intervals of 6 to 12 months to review their diagnosis.
1.2.7 Magnetic Resonance Volumetry

1.2.7.1 Volumetric MRI should not be used in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. [D (DS)]

1.2.8 Magnetic Resonance Spectroscopy

1.2.8.1 Magnetic resonance spectroscopy should not be used in the differential diagnosis of parkinsonian syndromes. [B (DS)]

1.2.9 Acute levodopa and apomorphine challenge tests

1.2.9.1 Acute levodopa and apomorphine challenges should not be used in the differential diagnosis of parkinsonian syndromes. [B (DS)]

1.2.10 Objective smell testing

1.2.10.1 Objective smell testing should not be used in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. [B (DS)]

1.3 Neuroprotection

1.3.1 Vitamin E

1.3.1.1 Vitamin E should not be used as a neuroprotective therapy in PD. [A]

1.3.2 Co-enzyme Q$_{10}$

1.3.2.1 Co-enzyme Q$_{10}$ should not be used as a neuroprotective therapy in PD, except in the context of clinical trials. [B]

1.3.3 Dopamine agonists

1.3.3.1 Dopamine agonists should not be used as neuroprotective therapies in PD, except in the context of clinical trials. [B]
1.3.4 MAO-B inhibitors

1.3.4.1 Monoamine oxidase B inhibitors should not be used as 
neuroprotective therapies in PD, except in the case of clinical trials. 
[B]

1.4 Symptomatic pharmacological therapy in PD

1.4.1 Levodopa

1.4.1.1 Levodopa can be used as a symptomatic treatment in early PD. [A]

1.4.2 Modified-release levodopa

1.4.2.1 Modified-release levodopa preparations should not be used to delay 
the onset of motor complications in early PD. [A]

1.4.3 Dopamine agonists

1.4.3.1 Dopamine agonists can be used as a symptomatic treatment in 
early PD. [A]

1.4.4 Monoamine oxidase B inhibitors

1.4.4.1 Monoamine oxidase B inhibitors can be used as a symptomatic 
treatment in early PD. [A]

1.4.5 Beta-adrenergic antagonists (beta-blockers)

1.4.5.1 Beta-adrenergic antagonists can be used in the symptomatic 
treatment of selected people with postural tremor in PD, but they 
should not be the drugs of first choice. [D (GPP)]

1.4.6 Amantadine

1.4.6.1 Amantadine can be used as a treatment for early PD but is not a 
drug of first choice. [D (GPP)]

1.4.7 Anticholinergics

1.4.7.1 Anticholinergics can be used as a symptomatic treatment typically 
in young people with early PD and severe tremor, but are not a drug
of first choice due to limited efficacy and the propensity for neuropsychiatric side effects. [B]

1.4.8 Choice of initial pharmacological therapy in early PD

1.4.8.1 It is not possible to identify a universal first choice drug therapy for people with early PD. The choice of drug first prescribed should take into account: [D (GPP)]

- clinical and lifestyle characteristics
- patient preference, after being informed of the short and long term benefits and drawbacks of the drug classes.

1.4.9 Modified-release levodopa

1.4.9.1 Modified-release levodopa preparations can be used to reduce motor complications in later PD but are not drugs of first choice. [B]

1.4.10 Dopamine agonists

1.4.10.1 Dopamine agonists can be used to reduce motor complications in later PD. [A]

1.4.11 Monoamine Oxidase B inhibitors

1.4.11.1 Monoamine oxidase B inhibitors can be used to reduce motor complications in later PD. [A]

1.4.12 Catechol-o-methyl transferase inhibitors

1.4.12.1 Catechol-O-methyl transferase inhibitors can be used to reduce off time in later PD.6 [A]

1.4.13 Amantadine

1.4.13.1 Amantadine can be used for the reduction of disabling dyskinesia in later PD. [C]

6 Tolcapone is only licensed for use in patients for whom entacapone has failed and it requires intensive monitoring of liver function. Tolcapone is only licensed for use in those who fail on entacapone and it requires intensive monitoring of liver function.
1.4.14  **Apomorphine**

1.4.14.1  Intermittent apomorphine injections can be used to reduce off time and dyskinesia in people with PD with severe motor complications. [B]

1.4.14.2  Continuous subcutaneous infusions of apomorphine can be used to reduce off time and dyskinesia in people with PD with severe motor complications. Its use should be restricted to specialist units with facilities for home monitoring. [D]

1.4.15  **Choice of adjuvant therapy in later PD**

1.4.15.1  It is not possible to identify a universal first choice adjuvant drug therapy for people with late PD. The choice of adjuvant drug first prescribed should take into account: [D (GPP)]

- clinical and lifestyle characteristics
- patient preference, after being informed of the short and long term benefits and drawbacks of the drug classes.

1.5  **Surgery for PD**

1.5.1  **STN stimulation**

1.5.1.1  Bilateral subthalamic stimulation can be used in people with PD who fit the following criteria: [D]

- motor complications which are refractory to best medical treatment
- biologically fit with no clinically significant active co-morbidity
- levodopa responsive
- no clinically significant active mental health problems (e.g. depression) or dementia.

1.5.2  **GPI stimulation**

1.5.2.1  Bilateral globus pallidus stimulation can be used in people with PD who fit the following criteria: [D (GPP)]
• motor complications which are refractory to best medical treatment
• biologically fit with no clinically significant active co-morbidity
• levodopa responsive
• no clinically significant active mental health problems (e.g. depression) or dementia.

1.5.3 Comparison of different types of deep brain stimulation

1.5.3.1 With the current evidence it is not possible to decide if subthalamic nucleus or globus pallidus stimulation is the preferred surgical option for people with PD. In considering the type of surgery, account should be taken of: [D (GPP)]

• the clinical condition and the lifestyle of the person with PD
• the views of the person with PD after being informed of the potential benefits and drawbacks of the different surgical procedures.

1.5.4 Thalamic stimulation

1.5.4.1 Thalamic deep brain stimulation is an option in people with PD who predominantly have severe disabling tremor where STN DBS cannot be performed. [D]

1.6 Non-motor complications of PD

1.6.1 Mental health problems

1.6.1.1 In the absence of any contra-indication, moderate to severe depression in PD should be treated with an SSRI class antidepressant. [D (GPP)]

1.6.2 Psychotic symptoms

1.6.2.1 All people with PD and psychosis should receive a general medical evaluation and any precipitating condition should be treated. [D (GPP)]
1.6.2.2 Consideration should be given to withdrawing gradually anti-parkinsonian medication which might have triggered psychosis in PD. [D (GPP)]

1.6.2.3 Mild psychotic symptoms in PD may not need to be actively treated if it is well tolerated by the patient. [D (GPP)]

1.6.2.4 Typical anti-psychotic drugs (e.g. phenothiazines, butyrophenones) should not be used in PD as they exacerbate the motor features of the condition. [D (GPP)]

1.6.2.5 Clozapine can be used in the treatment of psychotic symptoms in PD but registration with a mandatory monitoring scheme is required. [B]

1.6.3 Dementia

1.6.3.1 The guideline development group consider that the cholinesterase inhibitors are clinically effective for the treatment of cognitive impairment and/or psychotic symptoms arising from dementia in people with PD. A recommendation on their use will be made in the second consultation draft of this guideline following an analysis of their cost effectiveness. This additional work is being undertaken at the request of the National Institute for Health and Clinical Excellence.

1.6.4 Sleep disturbance

1.6.4.1 Modafinil can be used to treat daytime hypersomnolence in people with PD. [B]

1.6.5 Nocturnal akinesia

1.6.5.1 Controlled-release levodopa preparations can be used for nocturnal akinesia. [D (GPP)]
1.6.6 Falls

1.6.6.1 For guidance on the management of falls in PD refer to the NICE guideline “Falls: the assessment and prevention of falls in older people” (available from www.nice.org.uk/CG021). [NICE]

1.6.7 Autonomic disturbance

1.6.7.1 People with PD should be treated accordingly for the following autonomic disturbances: [D (GPP)]

- urinary dysfunction
- dysphagia
- constipation
- erectile dysfunction
- orthostatic hypotension
- excessive sweating
- sialorrhea.

1.7 Other key interventions

1.7.1 Parkinson’s Disease Nurse Specialist (PDNS) interventions

1.7.1.1 People with PD should have regular access to the following which can be part of specialist PD nursing:

- Monitor and alter medication appropriately. [A]
- Provide a continuing point of contact for support, including home visits. [C]
- Be a reliable source of information about clinical and social matters of concern to people with PD and their carers. [C]

1.7.2 Physiotherapy

1.7.2.1 Physical therapy should be available for people with PD and particular consideration should be given to the following: [B]

- gait re-education, balance and flexibility
• enhancement of aerobic capacity
• improvement of movement initiation
• improvement of functional independence, including mobility and activities of daily living
• provision of advice regarding safety in the home environment.

1.7.2.2 The Alexander Technique can be used to benefit people with PD by helping to make lifestyle adjustments that affect both the physical nature of the condition and the person’s attitudes to having PD. [B]

1.7.3 Occupational therapy

1.7.3.1 Occupational therapy should be available for people with PD and particular consideration should be given to the following: [D(GPP)]

• maintenance of employment, home-care and leisure activities
• improvement and maintenance of transfers and mobility
• improvement of personal self-care activities such as eating, drinking, washing and dressing
• environmental issues to improve safety and function
• cognitive assessment and appropriate intervention.

1.7.4 Speech and language therapy

1.7.4.1 Speech and language therapy should be available for people with PD and particular consideration should be given to the following:

• improvement of vocal loudness and pitch, including speech therapy programmes such as LSVT [B]
• teaching strategies to optimise speech intelligibility
• ensuring an effective means of communication is maintained throughout the course of the disease, including use of assistive technologies
• review of swallow safety and efficiency. [D (GPP)]
1.8 Palliative care in PD

1.8.1 End of life issues

1.8.1.1 Palliative care requirements of people with PD must be considered in all phases of the disease. [D (GPP)]

1.8.1.2 People with PD and carers should be given the opportunity to discuss end of life issues with appropriate health professionals. [D (GPP)]

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from www.nice.org.uk/page.aspx?o=213724

This guideline sets out best practice guidance for the diagnosis and management of PD in the NHS in England and Wales. Guidance will cover primary, secondary and tertiary healthcare settings. The patient population for whom this guidance is addressed are both sexes over 20 years of age, with a diagnosis of Parkinson’s disease or Parkinsonism. The guidance on treatment and management is aimed at people with idiopathic Parkinson’s disease only. The following areas covered in this guideline:

- Diagnosis and monitoring
- Communication and education
- Pharmacotherapy (prevention of progression)
- Pharmacotherapy (functional disability in early disease)
- Adjuvant pharmacotherapy (functional disability in late disease)
- Non-pharmacological management
- Neuropsychiatric conditions
- Palliative care
This guideline does not cover radical therapies that do not form common clinical management (e.g., fetal cell transplantation; stem cells; genes that code protein responsible for producing dopamine; drugs that block the action of glutamate; GDNF; viral transfection). In addition, co-morbidities in Parkinson’s disease will not be addressed (except where treatment will differ from treatment of these co-morbidities in patients without Parkinson’s disease). Finally, generic health problems where the care for people with Parkinson’s disease does not differ to that of the general population (e.g., constipation)

3 Implementation in the NHS

3.1 Resource implications

Local health communities should review their existing practice for Parkinson’s disease against this guideline. The review should consider the resources required to implement the recommendations set out in Section 1, the people and processes involved, and the timeline over which full implementation is envisaged. It is in the interests of people with PD that the implementation is as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly.

Information on the cost impact of this guideline in England is available on the NICE website and includes a template that local communities can use (www.nice.org.uk/CGXXXcosttemplate). [Note: the costing information will be available when the guideline is published.]

3.2 General

The Healthcare Commission considers implementation of clinical guidelines to be a developmental standard. The implementation of this guideline will build on the National Service Frameworks for Older People and Long-term Parkinson’s disease.
Conditions in England and Wales and should form part of the service development plans for each local health community in England and Wales.

This guideline should be used in conjunction with the following NICE Guidelines published or in development:

- Falls: The assessment and prevention of falls in older people
- Dementia: management of dementia, including use of antipsychotic medication in older people
- Depression: management of depression in primary and secondary care
- Multiple Sclerosis: Management of multiple sclerosis in primary and secondary care

3.3 Audit

Suggested audit criteria based on the key priorities for implementation are listed in Appendix D, and can be used to audit practice locally.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, on the basis of its review of the evidence. The Group regards these recommendations as the most important research areas to improve NICE guidance and patient care in the future. The Guideline Development Group’s full set of research recommendations is detailed in the full guideline (see Section 5).

4.1 Neuroprotection

Development of neuroprotective (disease-modifying) therapies for Parkinson's disease.

Why this is important

At present there is no agent which will slow down the progression of Parkinson's disease. Patients want such a 'cure' for their condition. The NHS
requires neuroprotectants to reduce the burden of disability caused by Parkinson's disease, thereby reducing the direct and indirect costs of caring for an increasing number of people with the condition.

A systematic trial programme examining these agents is ongoing in North America (NetPD). They are screening agents in small ‘futility studies’ using historical control data for decline in total UPDRS scores. The first futility study showed that both minocycline and GPI 1485 significantly delay decline in total UPDRS by more than 30% (K Kieburtz, personal communication).

The recent rasagiline delayed start design trial versus placebo raised the possibility that this may be a useful trial design to examine neuroprotection. Support for further surgical approaches to neuroprotection in Parkinson's disease should be considered.

4.2 Antidepressant therapy

Is treating mild to moderate depression in Parkinson's disease with an antidepressant cost effective?

Why this is important

Cross-sectional studies have shown that depression affects around 40% of patients with Parkinson's disease and has a major impact on quality of life. In most cases depression is mild to moderate in severity and is often missed by the clinician caring for the patient.

This study will screen secondary care Parkinson's disease clinic populations for mild to moderate depression. This will then be treated with any SSRI class antidepressant or no such treatment in an open-label fashion. This will be a large scale pragmatic trial.

If screening for and treating mild to moderate depression is cost effective, this will add to the evidence base for the management of depression in Parkinson's disease and will significantly change the next update of this guideline.
4.3 Physiotherapy and occupational therapy

Are physiotherapy and occupational therapy in Parkinson's disease cost effective?

Why this is important

The evidence to support the use of physiotherapy and occupational therapy in Parkinson's disease is poor and yet patients feel they are effective. Many patients are referred for such therapies in the NHS with little idea of their value and whether they have any long-term benefits. In contrast, many other patients cannot access such therapy due to poor provision of service.

A pragmatic trial should be performed in units that already have access to physiotherapy and occupational therapy services. This is likely to be in the elderly care setting since neurologists have poor access to such treatments.

If one or both therapies are cost effective then the provision of service needs to be increased.

Future trials will then need to examine what components of each therapy are effective and whether they are effective in the earlier stages of the disease.

4.4 Speech and language therapy

Is NHS speech and language therapy in Parkinson's disease cost effective?

Why this is important

The evidence to support the use of speech and language therapy in Parkinson's disease is poor and yet patients feel that it is effective. The provision of this service in the NHS is patchy with some patients not receiving speech and language therapy when it may be appropriate.

The trial must be preceded by survey work to identify current and best practice speech and language therapy for Parkinson's disease in the UK. Similar work has already been performed for physiotherapy and occupational therapy to prepare for analogous trials.
In this pragmatic trial, standard NHS speech and language therapy will be compared with no treatment. Whilst most Parkinson's disease units will have access to some speech and language therapy service, this may be insufficient for trial purposes so an NHS subvention will be required.

If speech and language therapy is cost effective, then the provision of service needs to be increased.

4.5 Diagnosis

Development of diagnostic investigations for Parkinson's disease and biomarkers to measure its progression.

Why this is important

The diagnosis of Parkinson's disease remains clinical. $^{123}$I-FP-CIT SPECT may be of additional help in a small proportion of clinically uncertain cases. The diagnostic error rate on presentation may be as high as 10% in expert hands which may lead to inappropriate therapy and distress following revision of the diagnosis.

A systematic approach led by university researchers and funded by Government would expedite the evaluation of existing and new diagnostic techniques.

The considerable debate surrounding biomarkers to measure the progression of Parkinson's disease has highlighted the need for further studies in this area. More work on existing techniques (e.g. SPECT and PET) is required and new potential markers (e.g. onset of falls) are an urgent requirement.

5 Other versions of this guideline

The National Institute for Health and Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Chronic Conditions. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in Appendix B.
Information about the independent Guideline Review Panel is given in Appendix C.

The booklet *The guideline development process: an overview for stakeholders, the public and the NHS* has more information about the Institute’s guideline development process. It is available from www.nice.org.uk/guidelinesprocess and copies can also be ordered by telephoning 0870 1555 455 (quote reference N0472).

### 5.1 Full guideline

The full guideline, *Parkinson’s disease: Diagnosis and Management in Primary and Secondary Care*, is published by the National Collaborating Centre for Chronic Conditions; it is available from [website details to be added], the NICE website (www.nice.org.uk/CGXXXfullguideline) and the website of the National Library for Health (www.nlh.nhs.uk). [Note: these details will apply to the published full guideline.]

### 5.2 Quick reference guide

A quick reference guide for health professionals is also available from the NICE website (www.nice.org/CGXXXquickrefguide) or from the NHS Response Line (telephone 0870 1555 455; quote reference number N0XXX). [Note: these details will apply when the guideline is published.]

### 5.3 Information for the public

A version of this guideline for people with Parkinson’s disease and their carers, and for the public, is available from the NICE website (www.nice.org.uk/CGXXXpublicinfo) or from the NHS Response Line (0870 1555 455); quote reference number N0xxx). [Note: these details will apply when the guideline is published.]

### 6 Related NICE guidance


NICE is in the process of developing the following guidance (details available from www.nice.org.uk):

- Dementia: management of dementia, including use of antipsychotic medication in older people. *NICE Clinical Guideline*. (Publication expected February 2007)

- Donepezil, rivastigmine, galantamine and memantine for the treatment of Alzheimer's disease (including a review of existing guidance no. 19) *NICE Technology Appraisal*. (Publication expected TBC.)

### 7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin before this if significant evidence that affects the guideline recommendations is identified. The updated guideline will be available within 2 years of the start of the review process.
Appendix A: Grading scheme

The classification of recommendations and the levels of evidence for intervention studies used in this guideline are adapted from the Scottish Intercollegiate Guidelines Network (SIGN 50: a guideline developers’ handbook), and summarised in the tables below and on page XX. The classification of recommendations and levels of evidence for the accuracy of diagnostic tests are adapted from The Oxford Centre for Evidence-Based Medicine levels of evidence (2001) and the Centre for Reviews and Dissemination report No. 4 (2001). They are summarised in the tables on pages XX and are being used on a pilot basis.
### Classification of recommendations on interventions

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Evidence</th>
</tr>
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</table>
| **A**                | • At least one meta-analysis, systematic review, or randomised controlled trial (RCT) that is rated as 1**, and is directly applicable to the target population, or  
• A systematic review of RCTs or a body of evidence that consists principally of studies rated as 1+, is directly applicable to the target population and demonstrates overall consistency of results, or  
• Evidence drawn from a NICE technology appraisal |
| **B**                | • A body of evidence that includes studies rated as 2**, is directly applicable to the target population and demonstrates overall consistency of results, or  
• Extrapolated evidence from studies rated as 1** or 1+ |
| **C**                | • A body of evidence that includes studies rated as 2+, is directly applicable to the target population and demonstrates overall consistency of results, or  
• Extrapolated evidence from studies rated as 2** |
| **D**                | • Evidence level 3 or 4, or  
• Extrapolated evidence from studies rated as 2+, or  
• Formal consensus |
| **D (GPP)**          | • A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group |

### Levels of evidence for intervention studies

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Type of evidence</th>
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<tbody>
<tr>
<td>1**</td>
<td>• High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>1+</td>
<td>• Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>1*</td>
<td>• Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
</tbody>
</table>
| 2**               | • High-quality systematic reviews of case–control or cohort studies  
• High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal |
| 2+                | • Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2–                | • Case–control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal |
| 3                 | • Non-analytical studies (for example, case reports, case series) |
| 4                 | • Expert opinion, formal consensus |
### Classification of recommendations on diagnostic tests

<table>
<thead>
<tr>
<th>Grade</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>A(DS)</td>
<td>• Studies with level of evidence Ia or Ib</td>
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<tr>
<td>B(DS)</td>
<td>• Studies with level of evidence II</td>
</tr>
<tr>
<td>C(DS)</td>
<td>• Studies with level of evidence III</td>
</tr>
<tr>
<td>D(DS)</td>
<td>• Studies with level of evidence IV</td>
</tr>
</tbody>
</table>

DS, diagnostic studies.

### Levels of evidence for studies of the accuracy of diagnostic tests

<table>
<thead>
<tr>
<th>Levels of evidence</th>
<th>Type of evidence</th>
</tr>
</thead>
</table>
| Ia                  | • Systematic review (with no or minor variations in the directions and degrees of results between studies) of level-1 studies, which are studies that use:  
  – a blind comparison of the test with a validated reference standard (gold standard)  
  – a sample of patients that reflects the population to whom the test would apply |
| Ib                  | • Level-1 studies |
| II                  | • Level-2 studies, which are studies that have only one of the following:  
  – the population is narrow (the sample does not reflect the population to whom the test would apply)  
  – a poor reference standard is used (defined as that where the ‘test’ is included in the ‘reference’, or where the ‘testing’ affects the ‘reference’)  
  – the comparison between the test and reference standard is not blind  
  – the study is a case–control study  
  • Systematic reviews of level-2 studies |
| III                 | • Level-3 studies, which are studies that have at least two of the features listed for level-2 studies  
  • Systematic reviews of level-3 studies |
| IV                  | • Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or ‘first principles’ |
Appendix B: The Guideline Development Group

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Ms Tara Sullivan
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Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

**Dr Peter Rutherford (Chair)**
Senior Lecturer in Nephrology, University of Wales College of Medicine

**Dame Helena Shovelton**
Chief Executive, British Lung Foundation

**Dr Rob Higgins**
Consultant in Renal and General Medicine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry

**Mrs Fiona Wise**
Chief Executive, Ealing Hospital NHS Trust

**Dr John Young**
Medical Director, Merck Sharp & Dohme (MSD)
Appendix D: Technical detail on the criteria for audit

The GDG recommend that healthcare commissioning organisations survey the views of people with PD regarding patient-views. This approach would enable the organisations to investigate the totality of the services and identify particular areas in need development using a patient-centred approach.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Exception</th>
<th>Definition of terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 100% of people with suspected Parkinson’s disease to be seen within 6 weeks of GP referral.</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2. 100% of people with Parkinson’s disease to be reviewed at 6 to 12 month intervals.</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3. 100% of people with Parkinson's disease to have access to Parkinson's disease specialist nursing.</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4. Rehabilitation to be made available in 100% of people with Parkinson's disease at each visit.</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5. A recommendation on the use of cholinesterase inhibitors for dementia in PD will be made in the second consultation draft of this guideline following an analysis of their cost effectiveness. This additional work is being undertaken at the request of the National Institute for Health and Clinical Excellence (See 1.6.3.1).</td>
<td>TBC</td>
<td>TBC</td>
</tr>
</tbody>
</table>
Appendix E: The algorithm

Disease progression

Diagnosis and early disease
Refer to a specialist who makes and reviews diagnosis:
- Using UK PD brain bank criteria
- Considers 123-FP-CIT SPECT
Specialist should review diagnosis at regular intervals

It is not possible to identify a universal first choice drug therapy for people with early PD. The choice of drug first prescribed should take into account:
- Clinical and lifestyle characteristics
- Patient preference

Throughout disease
Provide regular access to Parkinson's disease nurse specialist care, particularly to:
- Monitor and alter medication
- Provide continuing support including home visits

Consider access to therapies, particularly to:
- Maintain independence, including activities of daily living and ensure home safety
- Help balance, flexibility, gait, movement initiation
- Enhance aerobic activity
- Assess and manage communication and swallowing difficulties

Consider drugs for non-motor symptoms:
- For moderate to severe depression: SSRI therapy
- For dementia: cholinesterase inhibitors (TBC. See 1.6.3.1)
- For psychosis: clozapine therapy if necessary
- For daytime hypersomnia: modafinil
- For nocturnal akinesia: modified-release levodopa

Collaborative care decisions reached by taking into account:
- Patient preference and choice
- Clinical characteristics, patient lifestyle and interventions available

Communication

Late disease
It is not possible to identify a universal first choice adjuvant drug therapy for people with late PD. The choice of adjuvant drug prescribed should take into account:
- Clinical and lifestyle characteristics
- Patient preference

Consider surgery:
- Bilateral STN stimulation for suitable people refractory to best medical therapy
- Thalamic stimulation for people with severe tremor who are not suitable for STN stimulation

Provide communication and information about:
- PD services and entitlements
- Falls, self-help, palliative care and end-of-life issues