General

Guideline Title
Parkinson's disease in adults.

Bibliographic Source(s)


Guideline Status
This is the current release of the guideline.


This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment
National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

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Communication with People with Parkinson’s Disease and Their Carers

Communication with people with Parkinson’s disease should be aimed towards empowering them to participate in the judgements and choices about their own care. [2006]

In discussions, aim to achieve a balance between providing honest, realistic information about the
condition and promoting a feeling of optimism. [2006]

Because people with Parkinson’s disease may develop impaired cognitive ability, communication problems and/or depression, provide them with:

- 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. [2006]

Give family members and carers (as appropriate) information about the condition, their entitlement to a Carer’s Assessment and the support services available. [2006]

People with Parkinson’s disease should have a comprehensive care plan agreed between the person, their family members and carers (as appropriate), and specialist and secondary healthcare providers. [2006]

Offer people with Parkinson’s disease an accessible point of contact with specialist services. This could be provided by a Parkinson’s disease nurse specialist. [2006]

Advise people with Parkinson’s disease who drive that they should inform the Driver and Vehicle Licensing Agency (DVLA) and their car insurer of their condition when PD is diagnosed. [2006]

**Diagnosing Parkinson’s Disease**

**Definition and Differential Diagnosis**

Suspect Parkinson’s disease people presenting with tremor, stiffness, slowness, balance problems and/or gait disorders. [2006]

If Parkinson’s disease is suspected, refer people quickly and untreated to a specialist with expertise in the differential diagnosis of this condition. [2006, amended 2017]

**Clinical and Post-Mortem Diagnosis**

Diagnose Parkinson’s disease clinically, based on the UK Parkinson’s Disease Society Brain Bank Clinical Diagnostic Criteria. [2006]

Encourage healthcare professionals to discuss with people with Parkinson’s disease the possibility of donating tissue to a brain bank for diagnostic confirmation and research. [2006]

**Review of Diagnosis**

Review the diagnosis of Parkinson’s disease regularly, and reconsider it if atypical clinical features develop. (People diagnosed with Parkinson’s disease should be seen at regular intervals of 6 to 12 months to review their diagnosis.) [2006]

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

Consider $^{123}$I-FP-CIT [(N-omega-fluoropropyl-2beta-carboxymethoxy-3beta-(4-iodophenyl)tropane)] SPECT for people with tremor if essential tremor cannot be clinically differentiated from parkinsonism. [2006, amended 2017]

$^{123}$I-FP-CIT SPECT should be available to specialists with expertise in its use and interpretation. [2006]

**Positron Emission Tomography (PET)**

Do not use PET in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. [2006, amended 2017]

**Structural Magnetic Resonance Imaging (MRI)**

Do not use structural MRI to diagnose Parkinson’s disease. [2006, amended 2017]
Structural MRI may be considered in the differential diagnosis of other parkinsonian syndromes. [2006]

Magnetic Resonance Volumetry

Do not use magnetic resonance volumetry in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. [2006, amended 2017]

Magnetic Resonance Spectroscopy

Do not use magnetic resonance spectroscopy in the differential diagnosis of parkinsonian syndromes. [2006, amended 2017]

Acute Levodopa and Apomorphine Challenge Tests

Do not use acute levodopa and apomorphine challenge tests in the differential diagnosis of parkinsonian syndromes. [2006, amended 2017]

Objective Smell Testing

Do not use objective smell testing in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. [2006, amended 2017]

Pharmacological Management of Motor Symptoms

Before starting treatment for people with Parkinson's disease, discuss:

- The person's individual clinical circumstances, for example, their symptoms, comorbidities and risks from polypharmacy
- The person's individual lifestyle circumstances, preferences, needs and goals
- The potential benefits and harms of the different drug classes (see Table 1 in the original guideline document). [2017]

Antiparkinsonian medicines should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (for example, gastroenteritis, abdominal surgery) to avoid the potential for acute akinesia or neuroleptic malignant syndrome. [2006]

The practice of withdrawing people from their antiparkinsonian drugs (so called 'drug holidays') to reduce motor complications should not be undertaken because of the risk of neuroleptic malignant syndrome. [2006]

In view of the risks of sudden changes in antiparkinsonian medicines, people with Parkinson's disease who are admitted to hospital or care homes should have their medicines:

- Given at the appropriate times, which in some cases may mean allowing self-medication
- Adjusted by, or adjusted only after discussion with, a specialist in the management of Parkinson's disease. [2006]

First-line Treatment

Offer levodopa to people in the early stages of Parkinson's disease whose motor symptoms impact on their quality of life. [2017]

Consider a choice of dopamine agonists, levodopa or monoamine oxidase B (MAO-B) inhibitors for people in the early stages of Parkinson's disease whose motor symptoms do not impact on their quality of life. [2017]

Do not offer ergot-derived dopamine agonists as first-line treatment for Parkinson's disease. [2017]

Information and Support

When starting treatment for people with Parkinson's disease, give people and their family members and carers (as appropriate) oral and written information about the following risks, and record that the
discussion has taken place:

Impulse control disorders with all dopaminergic therapy (and the increased risk with dopamine agonists). Also see recommendations under "Managing and Monitoring Impulse Control Disorders as an Adverse Effect of Dopaminergic Therapy" below. Excessive sleepiness and sudden onset of sleep with dopamine agonists. Also see recommendations under "Daytime Sleepiness" below. Psychotic symptoms (hallucinations and delusions) with all Parkinson's disease treatments (and the higher risk with dopamine agonists). Also see recommendations under "Psychotic Symptoms (Hallucinations and Delusions)" below. [2017]

Adjuvant Treatment of Motor Symptoms

If a person with Parkinson's disease has developed dyskinesia and/or motor fluctuations, including medicines 'wearing off', seek advice from a healthcare professional with specialist expertise in Parkinson's disease before modifying therapy. [2017]

Offer a choice of dopamine agonists, MAO-B inhibitors or catechol-O-methyl transferase (COMT) inhibitors as an adjunct to levodopa for people with Parkinson's disease who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy, after discussing:

The person's individual clinical circumstances, for example, their Parkinson's disease symptoms, comorbidities and risks from polypharmacy
The person's individual lifestyle circumstances, preferences, needs and goals
The potential benefits and harms of the different drug classes (see Table 2 in the original guideline document). [2017]

Choose a non-ergot-derived dopamine agonist in most cases, because of the monitoring that is needed with ergot-derived dopamine agonists.¹ [2017]

Only consider an ergot-derived dopamine agonist¹ as an adjunct to levodopa for people with Parkinson's disease:

Who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy and
Whose symptoms are not adequately controlled with a non-ergot-derived dopamine agonist. [2017]

If dyskinesia is not adequately managed by modifying existing therapy, consider amantadine. [2017]

Do not offer anticholinergics to people with Parkinson's disease who have developed dyskinesia and/or motor fluctuations. [2017]

Managing and Monitoring Impulse Control Disorders as an Adverse Effect of Dopaminergic Therapy

Predictors for the Development of Impulse Control Disorders

Recognise that impulse control disorders can develop in a person with Parkinson's disease who is on any dopaminergic therapy at any stage in the disease course. [2017]

Recognise that the following are associated with an increased risk of developing impulse control disorders:

Dopamine agonist therapy.
A history of previous impulsive behaviours.
A history of alcohol consumption and/or smoking. [2017]

Information and Support

When starting dopamine agonist therapy, give people and their family members and carers (as appropriate) oral and written information about the following, and record that the discussion has taken place:
The increased risk of developing impulse control disorders when taking dopamine agonist therapy, and that these may be concealed by the person affected.

The different types of impulse control disorders (for example, compulsive gambling, hypersexuality, binge eating and obsessive shopping).
Who to contact if impulse control disorders develop.
The possibility that if problematic impulse control disorders develop, dopamine agonist therapy will be reviewed and may be reduced or stopped. [2017]

Discuss potential impulse control disorders at review appointments, particularly when modifying therapy, and record that the discussion has taken place. [2017]

Be aware that impulse control disorders can also develop while taking dopaminergic therapies other than dopamine agonists. [2017]

Managing Dopaminergic Therapy in People Who Have Developed an Impulse Control Disorder

If a person with Parkinson's disease has developed a problematic impulse control disorder, seek advice from a healthcare professional with specialist expertise in Parkinson's disease before modifying dopaminergic therapy. [2017]

Discuss the following with the person and their family members and carers (as appropriate):

- How the impulse control disorder is affecting their life.
- Possible treatments, such as reducing or stopping dopaminergic therapy.
- The benefits and disadvantages of reducing or stopping dopaminergic therapy. [2017]

When managing impulse control disorders, modify dopaminergic therapy by first gradually reducing any dopamine agonist. Monitor whether the impulse control disorder improves and whether the person has any symptoms of dopamine agonist withdrawal. [2017]

Offer specialist cognitive behavioural therapy targeted at impulse control disorders if modifying dopaminergic therapy is not effective. [2017]

Pharmacological Management of Non-motor Symptoms

Daytime Sleepiness

Advise people with Parkinson's disease who have daytime sleepiness and/or sudden onset of sleep not to drive (and to inform the DVLA of their symptoms) and to think about any occupation hazards. Adjust their medicines to reduce its occurrence, having first sought advice from a healthcare professional with specialist expertise in Parkinson's disease. [2017]

Consider modafinil to treat excessive daytime sleepiness in people with Parkinson's disease, only if a detailed sleep history has excluded reversible pharmacological and physical causes. [2017]

At least every 12 months, a healthcare professional with specialist expertise in Parkinson's disease should review people with Parkinson's disease who are taking modafinil. [2017]

Rapid Eye Movement Sleep Behaviour Disorder

Take care to identify and manage restless leg syndrome and rapid eye movement sleep behaviour disorder (RBD) in people with Parkinson's disease and sleep disturbance. [2017]

Consider clonazepam or melatonin to treat RBD if a medicines review has addressed possible pharmacological causes.² [2017]

Nocturnal Akinesia

Consider levodopa or oral dopamine agonists to treat nocturnal akinesia in people with Parkinson's disease. If the selected option is not effective or not tolerated, offer the other instead. [2017]
Consider rotigotine if levodopa and/or oral dopamine agonists are not effective in treating nocturnal akinesia. [2017]

Orthostatic Hypotension

If a person with Parkinson's disease has developed orthostatic hypotension, review the person's existing medicines to address possible pharmacological causes, including:

- Antihypertensives (including diuretics)
- Dopaminergics
- Anticholinergics
- Antidepressants. [2017]

Consider midodrine for people with Parkinson's disease and orthostatic hypotension, taking into account the contraindications and monitoring requirements (including monitoring for supine hypertension). [2017]

If midodrine is contraindicated, not tolerated or not effective, consider fludrocortisone\(^3\) (taking into account its safety profile, in particular its cardiac risk and potential interactions with other medicines). [2017]

Depression

For guidance on identifying, treating and managing depression in people with Parkinson's disease, see the NICE guideline on depression in adults with a chronic physical health problem. [2017]

Psychotic Symptoms (Hallucinations and Delusions)

At review appointments and following medicines changes, ask people with Parkinson's disease and their family members and carers (as appropriate) if the person is experiencing hallucinations (particularly visual) or delusions. [2017]

Perform a general medical evaluation for people with hallucinations or delusions, and offer treatment for any conditions that might have triggered them. [2017]

Do not treat hallucinations and delusions if they are well tolerated by the person with Parkinson's disease and their family members and carers (as appropriate). [2017]

Reduce the dosage of any Parkinson's disease medicines that might have triggered hallucinations or delusions, taking into account the severity of symptoms and possible withdrawal effects. Seek advice from a healthcare professional with specialist expertise in Parkinson's disease before modifying therapy. [2017]

Consider quetiapine\(^4\) to treat hallucinations and delusions in people with Parkinson's disease who have no cognitive impairment. [2017]

If standard treatment is not effective, offer clozapine to treat hallucinations and delusions in people with Parkinson's disease. Be aware that registration with a patient monitoring service is needed. [2017]

Be aware that lower doses of quetiapine\(^4\) and clozapine are needed for people with Parkinson's disease than in other indications. [2017]

Do not offer olanzapine to treat hallucinations and delusions in people with Parkinson's disease. [2017]

Recognise that other antipsychotic medicines (such as phenothiazines and butyrophenones) can worsen the motor features of Parkinson's disease. [2017]

For guidance on hallucinations and delusions in people with dementia, see interventions for non-cognitive symptoms and behaviour that challenges in people with dementia in the NICE guideline on dementia. [2017]
Parkinson's Disease Dementia

Offer a cholinesterase inhibitor\(^6\) for people with mild or moderate Parkinson's disease dementia. [2017]

Consider a cholinesterase inhibitor\(^7\) for people with severe Parkinson's disease dementia. [2017]

Consider memantine\(^8\) for people with Parkinson's disease dementia, only if cholinesterase inhibitors are not tolerated or are contraindicated. [2017]

For guidance on assessing and managing dementia, and supporting people living with dementia, see the NICE guideline on dementia\(^5\) [2017]

Drooling of Saliva

Only consider pharmacological management for drooling of saliva in people with Parkinson's disease if non-pharmacological management (for example, speech and language therapy; see "Speech and Language Therapy" below) is not available or has not been effective. [2017]

Consider glycopyrronium bromide\(^9\) to manage drooling of saliva in people with Parkinson's disease. [2017]

If treatment for drooling of saliva with glycopyrronium bromide\(^9\) is not effective, not tolerated or contraindicated (for example, in people with cognitive impairment, hallucinations or delusions, or a history of adverse effects following anticholinergic treatment), consider referral to a specialist service for botulinum toxin A\(^9\). [2017]

Only consider anticholinergic medicines other than glycopyrronium bromide\(^9\) to manage drooling of saliva in people with Parkinson's disease if their risk of cognitive adverse effects is thought to be minimal. Use topical preparations if possible (for example, atropine) to reduce the risk of adverse events. [2017]

Pharmacological Neuroprotective Therapy

Do not use vitamin E as a neuroprotective therapy for people with Parkinson's disease. [2006, amended 2017]

Do not use co-enzyme Q10 as a neuroprotective therapy for people with Parkinson's disease, except in the context of clinical trials. [2006, amended 2017]

Do not use dopamine agonists as neuroprotective therapies for people with Parkinson's disease, except in the context of clinical trials. [2006, amended 2017]

Do not use MAO-B inhibitors as neuroprotective therapies for people with Parkinson's disease, except in the context of clinical trials. [2006, amended 2017]

Non-pharmacological Management of Motor and Non-motor Symptoms

Parkinson's Disease Nurse Specialist Interventions

People with Parkinson's disease should have regular access to:

- Clinical monitoring and medicines adjustment
- A continuing point of contact for support, including home visits when appropriate
- A reliable source of information about clinical and social matters of concern to people with Parkinson's disease and their family members and their carers (as appropriate), which may be provided by a Parkinson's disease nurse specialist. [2006]

Physiotherapy and Physical Activity

Consider referring people who are in the early stages of Parkinson's disease to a physiotherapist with experience of Parkinson's disease for assessment, education and advice, including information about
Offer Parkinson's disease-specific physiotherapy for people who are experiencing balance or motor function problems. [2017]

Consider the Alexander Technique for people with Parkinson's disease who are experiencing balance or motor function problems. [2017]

Occupational Therapy

Consider referring people who are in the early stages of Parkinson's disease to an occupational therapist with experience of Parkinson's disease for assessment, education and advice on motor and non-motor symptoms. [2017]

Offer Parkinson's disease-specific occupational therapy for people who are having difficulties with activities of daily living. [2017]

Speech and Language Therapy

Consider referring people who are in the early stages of Parkinson's disease to a speech and language therapist with experience of Parkinson's disease for assessment, education and advice. [2017]

Offer speech and language therapy for people with Parkinson's disease who are experiencing problems with communication, swallowing or saliva. This should include:

- Strategies to improve the safety and efficiency of swallowing to minimise the risk of aspiration, such as expiratory muscle strength training (EMST)
- Strategies to improve speech and communication, such as attention to effort therapies. [2017]

Consider referring people for alternative and augmentative communication equipment that meets their communication needs as Parkinson's disease progresses and their needs change. [2017]

Nutrition

Consider referring people with Parkinson's disease to a dietitian for specialist advice. [2017]

Discuss a diet in which most of the protein is eaten in the final main meal of the day (a protein redistribution diet) for people with Parkinson's disease on levodopa who experience motor fluctuations. [2017]

Advise people with Parkinson's disease to avoid a reduction in their total daily protein consumption. [2017]

Advise people with Parkinson's disease to take a vitamin D supplement. See the NICE guideline on vitamin D for recommendations on vitamin D testing, and the NGC summaries of the NICE guidelines Falls in older people: assessing risk and prevention and Osteoporosis: assessing the risk of fragility fracture. [2017]

Do not offer creatine supplements to people with Parkinson's disease. [2017]

Advise people with Parkinson's disease not to take over-the-counter dietary supplements without first consulting their pharmacist or other healthcare professional. [2017]

Deep Brain Stimulation and Levodopa–Carbidopa Intestinal Gel

Deep Brain Stimulation

Offer people with advanced Parkinson's disease best medical therapy, which may include intermittent apomorphine injection and/or continuous subcutaneous apomorphine infusion. [2017]

Do not offer deep brain stimulation to people with Parkinson's disease whose symptoms are adequately controlled by best medical therapy. [2017]
Consider deep brain stimulation for people with advanced Parkinson's disease whose symptoms are not adequately controlled by best medical therapy. [2017]

Levodopa–Carbidopa Intestinal Gel

Levodopa–carbidopa intestinal gel is currently available through a National Health Service (NHS) England clinical commissioning policy. It is recommended that this policy is reviewed in light of this guidance. [2017]

Palliative Care

Information and Support

Offer people with Parkinson's disease and their family members and carers (as appropriate) opportunities to discuss the prognosis of their condition. These discussions should promote people's priorities, shared decision-making and patient-centred care. [2017]

Offer people with Parkinson's disease and their family members and carers (as appropriate) oral and written information about the following, and record that the discussion has taken place:

- Progression of Parkinson's disease
- Possible future adverse effects of Parkinson's disease medicines in advanced Parkinson's disease
- Advance care planning, including Advance Decisions to Refuse Treatment (ADRT) and Do Not Attempt Resuscitation (DNACPR) orders, and Lasting Power of Attorney for finance and/or health and social care
- Options for future management
- What could happen at the end of life
- Available support services, for example, personal care, equipment and practical support, financial support and advice, care at home and respite care. [2017]

When discussing palliative care, recognise that family members and carers may have different information needs from the person with Parkinson's disease. [2017]

Referral

Consider referring people at any stage of Parkinson's disease to the palliative care team to give them and their family members or carers (as appropriate) the opportunity to discuss palliative care and care at the end of life. [2017]

Footnotes

1. Medicines and Healthcare Products Regulatory Agency guidance (Drug safety update: volume 1, issue 12 2008) recommended warnings and contraindications for ergot-derived dopamine agonists as a result of the risk of fibrosis, particularly cardiac fibrosis, associated with chronic use. The risk of cardiac fibrosis is higher with cabergoline and pergolide than with the other ergot-derived dopamine agonists. Ergot-derived dopamine agonists should not be given to people who have had fibrosis in the heart, lungs or abdomen. Cabergoline, pergolide and bromocriptine are contraindicated for people with evidence of valve problems, and cabergoline and pergolide are restricted to second-line use in Parkinson's disease. Absence of cardiac fibrosis should be verified before treatment is started, and people must be monitored for signs of fibrosis on echocardiography before treatment is started, and then regularly during treatment.

2. At the time of publication (July 2017), clonazepam and melatonin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines [insert link] for further information.

3. At the time of publication (July 2017), fludrocortisone did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines [insert link] for further information.

4. At the time of publication (July 2017), quetiapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines [insert link] for further information.

5. The NICE guideline on dementia is being updated and is due to publish in June 2018. The dementia guideline update will include recommendations on the pharmacological management of dementia with Lewy bodies.

6. At the time of publication (July 2017), rivastigmine capsules are the only treatment with a UK marketing authorisation for this indication.
Donepezil, galantamine and rivastigmine patches did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines for further information.

At the time of publication (July 2017), cholinesterase inhibitors did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines for further information.

At the time of publication (July 2017), memantine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines for further information.

At the time of publication (July 2017), glycopyrronium bromide and botulinum toxin A did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council’s Prescribing guidance: prescribing unlicensed medicines for further information.

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

*Interventions That Must (or Must Not) Be Used*

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally they use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

*Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation*

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when they are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. They use similar forms of words (for example, 'Do not offer...') when they are confident that an intervention will not be of benefit for most patients.

*Interventions That Could Be Used*

The GDG uses 'consider' when they are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient’s values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Parkinson's disease overview" is provided on the NICE Web site.

Scope
Disease/Condition(s)
Parkinson's disease

Guideline Category
Diagnosis
Evaluation
Management
Treatment

Clinical Specialty
Geriatrics
Neurological Surgery
Neurology
Nursing
Physical Medicine and Rehabilitation
Psychiatry
Speech-Language Pathology

Intended Users
Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Hospitals
Nurses
Occupational Therapists
Patients
Physical Therapists
Physicians
Public Health Departments
Social Workers
Speech-Language Pathologists

Guideline Objective(s)
To improve care from the time of diagnosis, including monitoring and managing symptoms, providing information and support, and palliative care
Target Population

Adults with a suspected or confirmed diagnosis of Parkinson's disease

Note: This guideline does not cover people with juvenile-onset Parkinson's disease.

Interventions and Practices Considered

Diagnosis/Evaluation

Differential diagnosis
Clinical and post-mortem diagnosis
Review of diagnosis
Imaging
  Single photon emission computed tomography (SPECT)
  Positron emission tomography (PET) for differential diagnosis (in clinical trials only)
  Structural magnetic resonance imaging (MRI) for differential diagnosis
  Magnetic resonance volumetry for differential diagnosis (in clinical trials only)
Objective smell testing for differential diagnosis (in clinical trials only)

Management/Treatment

Communication with patients and carers, including development of a comprehensive care plan
Pharmacological management of motor symptoms
  First-line treatment (levodopa, dopamine agonists, monoamine oxidase B [MAO-B] inhibitors)
  Information and support
  Adjuvant treatment of motor symptoms
Managing and monitoring impulse control disorders (adverse effect of dopaminergic therapy)
Pharmacological management of non-motor symptoms
Pharmacological neuroprotective therapy
Non-pharmacological management of motor and non-motor symptoms
  Physiotherapy and physical activity
  Occupational therapy
  Speech and language therapy
  Nutrition
Deep brain stimulation
Levodopa-carbidopa intestinal gel
Palliative care
  Information and support
  Referral

Note: The following were considered but not recommended: magnetic resonance spectroscopy, acute levodopa and apomorphine challenge tests.

Major Outcomes Considered

Patient-related Outcomes

Mortality
Adverse events
Resource use and cost
Cognitive function (Addenbrooke's cognitive examination revised [ACE111], Montreal Cognitive Assessment [MOCA])
Quality of life (Parkinson's disease questionnaire 39 [PDQ-39], EQ5D)
Disease severity (Unified Parkinson's Disease Rating Scale [UPDRS], Webster disability score)
Non-motor features (Non-motor symptoms questionnaire [NMS Quest], Parkinson's disease sleep scale [PDSS2])

**Carer-related Outcomes**

- Impact on carer (Family Burden Interview, Caregiver Burden Inventory)
- Need for respite care
- Resilience (Dispositional Resilience Scale, Resilience Scale)
- Communication between carers and healthcare staff (Decision Making Involvement Scale)
- Family-related quality of life (Family Hardiness Index)
- Family relationships (Family Strain Scale)

**Methodology**

**Methods Used to Collect/Select the Evidence**

**Searches of Electronic Databases**

**Description of Methods Used to Collect/Select the Evidence**

Note from the National Guideline Clearinghouse (NGC): See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

**Scoping Search Strategies**

**Scoping Searches**

Scoping searches were undertaken on the Web sites and databases listed in Appendix I in June 2014 to provide information for scope development and project planning. Browsing or simple search strategies were employed.

**Review Question Search Strategies**

**Sources Searched for the Guideline**

- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (Wiley)
- Health Technology Assessment Database – HTA (Wiley)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)
- PsycINFO (Ovid) (for review question 21)

**Identification of Evidence for Clinical Questions**

The searches were conducted between October 2014 and February 2016. Re-run searches were carried out in June 2016.

For this guideline the population was limited to people with confirmed Parkinson's disease. Any other populations (hypokinetic rigid syndrome, shaking palsy, paralysis) were excluded.

The MEDLINE search strategies are presented in Appendix I. These were translated for use in all of the other databases.

Refer to the review protocols in Appendix C for clinical questions and the inclusion/exclusion criteria for
each question.

Health Economics Search Strategy

Economic Evaluations and Quality of Life Data

Sources searched to identify economic evaluations

- NHS Economic Evaluation Database – NHS EED (Wiley)
- Health Economic Evaluations Database – HEED (Wiley) (until December 2014)
- EconLit (Ovid) (used for re-run searches as NHS EED became a legacy database)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

Search filters to retrieve economic evaluations and quality of life papers were appended to the population search terms in MEDLINE, MEDLINE In-Process and EMBASE to identify relevant evidence.

Searches were carried out between October 2014 and February 2016. Re-run searches took place in June 2016.

The MEDLINE economic evaluations and quality of life search filters are presented in Appendix I. They were translated for use in the MEDLINE In-Process and EMBASE databases.

Number of Source Documents

Refer to the "Evidence review" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for numbers of studies included for each clinical question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

For interventional evidence, Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of evidence for the selected outcomes as specified in 'The guidelines manual (2012)' (see the "Availability of Companion Documents" field). For qualitative evidence, modified GRADE was used to assess the quality of evidence for the selected outcomes as specified in 'The guidelines manual (2012)'.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Evidence Synthesis and Meta-analyses
Where possible, meta-analyses were conducted to combine the results of studies for each outcome. For continuous outcomes, where change from baseline data were reported in the trials and were accompanied by a measure of spread (for example standard deviation), these were extracted and used in the meta-analysis. Where measures of spread for change from baseline values were not reported, the corresponding values at study end were used and were combined with change from baseline values to produce summary estimates of effect. These studies were assessed to ensure that baseline values were balanced across the treatment groups; if there were significant differences at baseline these studies were not included in any meta-analysis and were reported separately.

**Interventional Evidence**

**Quality Assessment**

Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of evidence for the selected outcomes as specified in 'The guidelines manual (2012)'. Where randomised controlled trials (RCTs) are available, these are initially rated as high quality and the quality of the evidence for each outcome was downgraded or not from this initial point. If non-RCT evidence was included for intervention-type systematic reviews then these are initially rated a low quality and the quality of the evidence for each outcome was downgraded or not from this point.

**Methods for Combining Intervention Evidence**

Meta-analysis of interventional data was conducted with reference to the Cochrane Handbook for Systematic Reviews of Interventions.

Dichotomous outcomes were pooled on the relative risk scale (using the Mantel–Haenszel method).

Fixed- and random-effects models (der Simonian and Laird) were fitted for all syntheses, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models were the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model were clearly not met (defined as $I^2 \geq 50\%$, and thus the presence of significant heterogeneity), random-effects results are presented.

Pairwise meta-analyses were performed in Cochrane Review Manager v5.3 or R v3.2.2, using identical methods across the two programs.

**GRADE for Pairwise Meta-analyses for Interventional Evidence**

The quality of the evidence for each outcome was downgraded where appropriate for the reasons outlined in Table 1 in the full version of the guideline.

**Methods for Combining Direct and Indirect Evidence (Network Meta-analysis)**

Conventional pairwise meta-analysis involves the statistical combination of direct evidence about pairs of interventions that originate from 2 or more separate studies (for example, where there are two or more studies comparing A vs B).

In situations where there are more than 2 interventions, pairwise meta-analysis of the direct evidence alone is of limited use. This is because multiple pairwise comparisons need to be performed to analyse each pair of interventions in the evidence, and these results can be difficult to interpret. Furthermore, direct evidence about interventions of interest may not be available. For example studies may compare A vs B and B vs C, but there may be no direct evidence comparing A vs C. Network meta-analysis (NMA) overcomes these problems by combining all evidence into a single, internally consistent model, synthesising data from direct and indirect comparisons, and providing estimates of relative effectiveness for all comparators and the ranking of different interventions.

**Synthesis**

Two methods of network meta-analysis were used in this guideline.
For Section 7.5 in the full version of the guideline, hierarchical Bayesian NMA was performed using WinBUGS version 1.4.3. The models used reflected the recommendations of the NICE Decision Support Unit's Technical Support Documents (TSDs) on evidence synthesis, particularly TSD 2 ('A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials'; see http://scharr.dept.shef.ac.uk/nicedsu/). The WinBUGS code provided the appendices of TSD 2 was used without substantive alteration to specify synthesis models.

Results were reported summarising 10,000 samples from the posterior distribution of each model, having first run and discarded 50,000 'burn-in' iterations. Three separate chains with different initial values were used.

Non-informative prior distributions were used in all models. Trial-specific baselines and treatment effects were assigned N(0, 1000) priors, and the between-trial standard deviations used in random-effects models were given U(0, 5) priors. These are consistent with the recommendations in TSD 2 for dichotomous outcomes.

Fixed- and random-effects models were explored for each outcome, with the final choice of model based on deviance information criterion (DIC): if DIC was at least 3 points lower for the random-effects model, it was preferred; otherwise, the fixed effects model was considered to provide an equivalent fit to the data in a more parsimonious analysis, and was preferred.

For Sections 6.1, 0 and 8 in the full version of the guideline, NMAs were undertaken using the netmeta package in R3.2.2. This uses a graph-theoretical method which is mathematically equivalent to frequentist network meta-analysis (Rücker 2012). Inconsistency was assessed using the overall $I^2$ value for the whole network, which is a weighted average of the $I^2$ value for all comparisons where there are multiple trials (both direct and indirect), and random-effects models were used if the $I^2$ value was above 50% (as for pairwise meta-analyses, this was interpreted as showing the assumption of a shared underlying mean was not met, and therefore a fixed-effects model was inappropriate).

Because different approaches and software had been applied, sensitivity analysis was undertaken to establish whether this might have led to any substantive difference in output. Specimen dichotomous and continuous NMAs from Section 7.5 in the full version of the guideline, were rerun in the frequentist framework, and generated results that were materially indistinguishable from the Bayesian version.

Applying GRADE to Network Meta-analysis

The use of GRADE to assess the quality of studies addressing a particular review question for pairwise comparisons of interventions is relatively established. However, the use of GRADE to assess the quality of evidence across a network meta-analysis is still a developing methodology. While most criteria for pairwise meta-analyses still apply, it is important to adapt some of the criteria to take into consideration additional factors, such as how each 'link' or pairwise comparison within the network applies to the others. As a result, the following was used when modifying the GRADE framework to a network meta-analysis.

Risk of Bias

In addition to the usual criteria to assess the risk of bias or 'limitations' of studies for each pairwise analysis within a network, the risk of bias was assessed for each direct comparison and assessed to see how it would affect the indirect comparisons. In addition, there was an assessment of treatment effect modifiers to see if they differed between links in the network.

For network meta-analyses with a large proportion of studies that were judged to be susceptible to bias, some downgrading decision rules were applied.

If 50% or more studies in the network were inadequate or unclear for a particular parameter of quality, the outcome was downgraded by 1 level.
As with pairwise meta-analyses, studies with differences in concomitant treatment between groups, or which did not report concomitant treatment between groups (where permitted), were treated with caution. Additionally, if there were differences in concomitant treatment among the studies included in different links across the network, the overall outcome was downgraded.

Inconsistency

Inconsistency was assessed for the heterogeneity of individual pairwise comparisons in the network, and also between direct and indirect comparisons where both were available (that is, where there were 'loops' in the network).

Heterogeneity across studies for each direct pairwise meta-analysis was assessed using $I^2$. This allowed for the assessment of heterogeneity within the included studies using the following decision rules:

- If there was considerable heterogeneity for 1 link or more in a network, the outcome was downgraded 1 level.
- If there was more than 1 link in the network with considerable, substantial or moderate heterogeneity, consideration was given to downgrading 2 levels.

To assess for consistency in each pairwise comparison where both direct and indirect evidence are available, the values of the direct and indirect estimates were compared to see if they were similar.

The overall values of $I^2$ (which combines heterogeneity between multiple studies of the same comparison and inconsistency between direct and indirect comparisons) and tau were also assessed to compare heterogeneity across the network.

Indirectness

As with pairwise meta-analyses, studies included in a network were assessed for how well they fit the PICO (population, intervention, comparator, outcome) specified in the review protocol.

Imprecision

Imprecision was assessed for a number of variables:

- Sufficient head-to-head trials in the network
- Sufficient number of studies to form the network (if there was a high proportion of 'links' formed with only 1 trial, the outcome was downgraded)
- Overall certainty/uncertainty of the effect estimates (size of confidence/credible intervals, including for each drug compared with the reference option, and size of confidence/credible intervals for the overall rankings within the network)
- For networks, imprecision was considered around both the direct and indirect effect estimates

When assessing imprecision for pairwise comparisons, or for networks with only 1 trial for all 'links' in the network, the confidence interval around the direct estimate was used.

Minimally Important Differences (MIDs)

The following published MIDs for Parkinson's outcomes in the research literature were adopted for this guideline:

- PDQ39 single index: 1.6 points (Peto et al., 2001)
- UPDRS-II (activities of daily living): 3 points (Schrag et al., 2006)
- UPDRS-III (motor): between 3.25 (Horváth et al., 2015) and 5 points (Schrag et al., 2006)

For some outcomes (EQ5D, Zarit carer burden interview, on time and off time), the committee agreed that any statistically significant differences in changes from baseline would also be clinically meaningful. The committee also agreed that it was not sensible to attempt to define a population-level MID for changes in Hoehn and Yahr (HY) stage: individuals can only move by whole or half-points on the scale.
(and any such changes are reflective of obviously meaningful deterioration/improvement), but a population-level mean change of a fraction of a point is more difficult to interpret. Therefore, the committee decided it was reasonable to conclude that any treatments that result in measurable, statistically significant differences in mean HY score must have affected a nontrivial proportion of people by a nontrivial amount.

Qualitative Evidence

Modified GRADE was used to assess the quality of evidence for the selected outcomes as specified in 'The guidelines manual (2012)'. All qualitative design studies (surveys and interviews) were initially graded as high-quality evidence if well conducted, and then downgraded according to the standard GRADE criteria (risk of bias, inconsistency and indirectness) as detailed in Table 2 in the full version of the guideline. Imprecision was not applicable here as qualitative data do not provide a measure of variation (standard deviation).

Methods for Combining Qualitative Evidence

Due to the relatively few papers identified for qualitative evidence, it was deemed not appropriate to synthesise them. Instead, a narrative summary of the key themes or illustrative quotes of each paper were provided.

GRADE for Qualitative Evidence

GRADE has not been developed for use with qualitative studies; therefore a modified approach was applied using the GRADE framework.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

This guideline was developed in accordance with the process set out in 'The guidelines manual (2012)' (see the "Availability of Companion Documents" field). There is more information about how NICE clinical guidelines are developed on the NICE Web site.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, National Institute for Health and Care Excellence (NICE) expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation.
Occasionally they use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when they are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. They use similar forms of words (for example, 'Do not offer...') when they are confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when they are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient’s values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

Refer to Appendix F (see the "Availability of Companion Documents" field) for the full health economics report.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Refer to Sections 11 and 12 of 'The guidelines manual (2012)' for information on guideline review process.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The type of evidence supporting each review area is detailed in the full version of the guideline (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Refer to Table 5 in the full version of the guideline for benefits and harms of levodopa, dopamine agonists, and monoamine oxidase B (MOA-B) inhibitors.
- Refer to Table 7 in the full version of the guideline for benefits and harms of dopamine agonists, MOA-B inhibitors, catechol-O-methyl transferase (COMT) inhibitors, and amantadine.
Potential Harms

- Hallucinations and delusions are common side-effects of many anti-parkinsonian medicines.
- Refer to Table 5 in the full version of the guideline for benefits and harms of levodopa, dopamine agonists, and monoamine oxidase B (MOA-B) inhibitors.
- Refer to Table 7 in the full version of the guideline for benefits and harms of dopamine agonists, MOA-B inhibitors, catechol-O-methyl transferase (COMT) inhibitors, and amantadine.
- Subcutaneous apomorphine infusion is widely regarded as an effective treatment for Parkinson's disease. Also usually provided by using a proprietary kit, the infusion can be associated with improved control of symptoms compared with best oral medication, but adverse effects of the infusion, including injection site reactions, are common.

Contraindications

- The summary of product characteristics (SPC) for amantadine states that it is contraindicated during pregnancy.
- Medicines and Healthcare Products Regulatory Agency guidance (Drug safety update: volume 1, issue 12 2008) recommended warnings and contraindications for ergot-derived dopamine agonists as a result of the risk of fibrosis, particularly cardiac fibrosis, associated with chronic use. The risk of cardiac fibrosis is higher with cabergoline and pergolide than with the other ergot-derived dopamine agonists. Ergot-derived dopamine agonists should not be given to people who have had fibrosis in the heart, lungs, or abdomen. Cabergoline, pergolide and bromocriptine are contraindicated for people with evidence of valve problems, and cabergoline and pergolide are restricted to second-line use in Parkinson's disease. Absence of cardiac fibrosis should be verified before treatment is started, and people must be monitored for signs of fibrosis on echocardiography before treatment is started, and then regularly during treatment.

Qualifying Statements

- The recommendations in this guideline represent the view of the National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The application of the recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.
- Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should
do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

- Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Implementation of the Guideline

Description of Implementation Strategy

Putting This Guideline into Practice

The National Institute for Health and Care Excellence (NICE) has produced tools and resources to help put this guideline into practice (see also the "Availability of Companion Documents" field).

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

- Raise awareness through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.
- Identify a lead with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.
- Carry out a baseline assessment against the recommendations to find out whether there are gaps in current service provision.
- Think about what data you need to measure improvement and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.
- Develop an action plan, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.
- For very big changes include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.
Implement the action plan with oversight from the lead and the project group. Big projects may also need project management support.

Review and monitor how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See the into practice pages for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley.

Implementation Tools

Clinical Algorithm

Patient Resources

Resources

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)


Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released
Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

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Guideline Committee

Guideline Development Group

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Financial Disclosures/Conflicts of Interest

The effective management of conflicts of interests is an essential element in the development of the guidance and advice that National Institute for Health and Care Excellence (NICE) publishes. Please refer to the NICE Web site for the Policy on Conflicts of Interest.

Guideline Development Group (GDG) disclosures are available in Appendix A (see the "Availability of Companion Documents" field).

Guideline Status
This is the current release of the guideline.


This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Clinical Excellence (NICE) Web site. Also available for download in ePub or eBook formats from the NICE Web site.

Availability of Companion Documents

The following are available:


Patient Resources

The following is available:


Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline’s content.

NGC Status

This NGC summary was completed by ECRI on March 25, 2009. This summary was updated by ECRI Institute on May 20, 2011 following the U.S. Food and Drug Administration advisory on antipsychotic drugs. This summary was updated by ECRI Institute on September 21, 2017. The guideline developer agreed to not review the content.
This NEATS assessment was completed by ECRI Institute on August 16, 2017. The information was verified by the guideline developer on August 24, 2017.

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