Complete Summary

GUIDELINE TITLE

Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). Part II: late (complicated) Parkinson´s disease.

BIBLIOGRAPHIC SOURCE(S)

Horstink M, Tolosa E, Bonuccelli U, Deuschl G, Friedman A, Kanovsky P, Larsen JP, Lees A, Oertel W, Poewe W, Rascol O, Sampaio C, European Federation of Neurological Societies, Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the EFNS and the MDS-ES. Part II: late (complicated) Parkinson's disease. Eur J Neurol 2006 Nov;13(11):1186-202. [196 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

The guidelines will need to be updated no later than 2009.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- June 17, 2008, Antipsychotics (conventional and atypical]): The U.S. Food and Drug Administration (FDA) notified healthcare professionals that both conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis. The prescribing information for all antipsychotic drugs will now include information about the increased risk of death in the BOXED WARNING and WARNING sections.
- December 04, 2007, Desmopressin Acetate (DDAVP, DDVP, Minirin, & Stimate): New information has been added to the existing boxed warning in Desmopressin's prescribing information about potential increased risk for severe hyponatremia and seizures.
- October 18, 2007, PDE5 inhibitors, Viagra (sildenafil citrate), Levitra (vardenafil HCL), Cialis (tadalafil): The PRECAUTION and updated Adverse Reactions Sections of the approved product labeling for Viagra, Levitra, and Cialis were revised in response to reports of sudden decreases or loss of hearing.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Late (complicated) Parkinson's disease (PD) which may include the following:

- Motor fluctuations
- Dyskinesia
- Dementia
- Psychosis
- Depression
- Orthostatic hypotension
- Urinary disturbance
- Gastrointestinal motility problems
- Erectile dysfunction

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurological Surgery
Neurology
Pharmacology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide evidence-based recommendations for the management of late (complicated) Parkinson's disease (PD) based on a review of the literature

TARGET POPULATION

Patients with late (complicated) Parkinson's disease (PD)

INTERVENTIONS AND PRACTICES CONSIDERED

Management of Motor Complications

Motor Fluctuations

1. Adjusting levodopa dosing
2. Switching from standard to controlled release (CR) formulation of levodopa
3. Adding catechol-O-methyltransferase (COMT) inhibitors, monoamine oxidase isoenzyme type B (MAO-B) inhibitors, dopamine agonists, amantadine, or an anticholinergic
4. Reduction or redistribution of total daily dietary proteins
5. Deep brain stimulation (DBS) of the subthalamic nucleus (STN)
6. Subcutaneous apomorphine as penjet or pump
7. Alternative delivery routes or alternative formulations of levodopa

Dyskinesia

1. Adding amantadine or atypical antipsychotics
2. Reducing individual levodopa dose size
3. Discontinuing or reducing doses of MAO-B inhibitors or COMT inhibitors
4. Apomorphine continuous subcutaneous infusion
5. DBS of the STN
6. Botulinum toxin (off period and early morning dystonia)

Management of Neuropsychiatric Complications

Dementia

1. Discontinuing potential aggravators
2. Adding cholinesterase inhibitors

Psychosis

1. Controlling trigger factors
2. Reducing polypharmacy
3. Reducing antiparkinsonian drugs
4. Adding atypical antipsychotics or cholinesterase inhibitors

Depression

1. Optimizing antiparkinsonian therapy
2. Tricyclic antidepressants
3. Selective serotonin reuptake inhibitors (SSRIs)

Management of Autonomic Dysfunction

Orthostatic Hypotension

1. General measures such as avoiding aggravating factors, increasing salt intake, head-up tilt of the bed, elastic stockings, highlight postprandial effects
2. Midodrine or fludrocortisone

Urinary Disturbance

1. General measures for treating urinary urgency and incontinence
2. Peripherally acting anticholinergics

Gastrointestinal Motility Problems

1. General measures for treating constipation (diet, laxatives)
2. Reducing or discontinuing drugs with anticholinergic activity
3. Adding domperidone

Erectile Dysfunction

Sildenafil

Note: Refer to the original guideline document for more details including information on medications that were considered but not recommended due to ineffectiveness, insufficient data, or serious adverse effects.

MAJOR OUTCOMES CONSIDERED

- Effectiveness of treatment in improving motor complications, neuropsychiatric complications, and autonomic dysfunction
- Adverse effects of pharmacological and surgical interventions

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were carried out in MEDLINE, the full database of the Cochrane Library, and the International Network of Agencies for Health Technology Assessment (INAHTA), up to the first complete draft in May 2005. During the following discussions, relevant articles could be added up to January 2006. The databases were also searched for existing guidelines and management reports, and requests were made to European Federation of Neurological Societies (EFNS) societies for their National Guidelines. Non-European guidelines were searched for using

MEDLINE. Reference lists from (review) articles and other reports were also checked.

NUMBER OF SOURCE DOCUMENTS

Not stated

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

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Classification of scientific evidence and the rating of recommendations are made according to the European Federation of Neurological Societies (EFNS) guidance.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Classification of scientific evidence and the rating of recommendations are made according to the European Federation of Neurological Societies (EFNS) guidance. This report focuses on the highest levels of evidence available and, in cases where there is insufficient scientific evidence, a consensus statement ('good practice point') is made.

After an initial meeting, held to discuss the principal format and methodology, six members of the task force provided a first draft of the report, which was commented on by all members via e-mail and through discussion at four EFNS and Movement Disorder Society (MDS) congress meetings, until a consensus was reached (informative consensus approach). At a final meeting in September 2005, the six primary authors finalized the text for approval by all members of the task force.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating of Recommendations

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good practice points In cases where there is insufficient scientific evidence, a consensus statement ('good practice point') is made.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see "Availability of Companion Documents" field in this summary).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C, good practice point) are defined at the end of the "Major Recommendations" field.

Symptomatic Control of Motor Complications

Motor Fluctuations

Wearing-off

- *Adjust levodopa dosing*. In an early phase, when motor fluctuations are just becoming apparent, adjustments in the frequency of levodopa dosing during the day, tending to achieve four to six daily doses, might attenuate the wearing-off (**good practice point**).
- *Switch from standard levodopa to controlled release (CR) formulation*. CR formulations of levodopa can also improve wearing-off (**level C**).
- Add catechol-O-methyltransferase (COMT) inhibitors or monoamine oxidase isoenzyme type B (MAO-B) inhibitors. No recommendations can be made on which treatment should be chosen first – on average, all reduce OFF time by about 1 to 1.5 h/day. The only published direct comparison (**level A**) showed no difference between entacapone and rasagiline. Tolcapone is potentially hepatotoxic, and is only recommended in patients failing on all other available medications (see Part I of the original guidelines). Rasagiline should not be added to selegiline (**level C**) because of cardiovascular safety issues.
- *Add dopamine agonists*. Oral dopamine agonists are efficacious in reducing OFF time in patients experiencing wearing-off. Currently, no dopamine agonist has proven better than another, but switching from one agonist to another can be helpful in some patients (**level B/C**). Pergolide* and other ergot agonists are reserved for second-line treatment, because of their association with valvulopathy.

  ***Note from the National Guideline Clearinghouse (NGC)**: On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the U.S. Food and Drug Administration (FDA) Web site for more information.

- *Add amantadine or an anticholinergic*. In patients with disabling recurrent OFF symptoms that fail to improve further with the above mentioned strategies, the addition of an anticholinergic (in younger patients), or amantadine, may improve symptoms in some cases (**good practice point**).

Most patients will eventually receive a combination of several of these treatments because a single treatment fails to provide adequate control of fluctuations. There is insufficient evidence on the combination of more than two strategies and the choice of drugs is mainly based on safety, tolerability and ease of use. All the above options may provoke or increase dyskinesias, but usually this can be managed by decreasing the levodopa dose.

Note: Reduction or redistribution of total daily dietary proteins may reduce wearing-off effects in some patients. Restricting protein intake to one meal a day may facilitate better motor responses to levodopa following other daily meals during the day. A more practical approach could be to take levodopa on an empty stomach about 1 h before or at least 1 h after, each meal (**class IV**).

If oral therapy fails, the following strategies can be recommended.

- Deep brain stimulation (DBS) of the subthalamic nucleus (STN) (**level B**).
- Subcutaneous apomorphine as penject (**level A**) or pump (**level C**).
- Alternative delivery routes or alternative formulations of levodopa:
    - Oral dispersible levodopa might be useful for delayed ON (**level C**).
    - Levodopa/carbidopa enteric gel administered through percutaneous gastrostomy (PEG) can also be considered to stabilize patients with refractory motor fluctuations (**level B**).

<u>Unpredictable ON-OFF</u>

In the large studies of wearing-off, patients with unpredictable ON–OFF were either not included or constituted <5% of the total population. Therefore, insufficient evidence exists to conclude whether the results that are valid for wearing-off are also valid for unpredictable ON–OFF. There are only a few small studies specifically including patients suffering from unpredictable ON–OFF, although studies evaluating continuous dopaminergic stimulation also include patients suffering concomitantly from wearing-off and unpredictable ON–OFF. The same is true for concomitant dyskinesia, which frequently occurs during the ON phase of ON–OFF. Thus, there is insufficient evidence to conclude on specific strategies for ON–OFF, although the strategies described for dyskinesia and for wearing-off should be considered for unpredictable ON–OFF (**good practice point**).

Unpredictable ON–OFF can have several components, one of which is delayed ON and, for which, oral dispersible levodopa formulations could have some value (**level C**).

Note: By shortening the interval between levodopa doses to prevent wearing-off, the relation between the moment of intake of each dose and the subsequent motor effect can become difficult to disclose, especially when inadequate absorption also occurs. The resulting pattern of fluctuation and dyskinesia may falsely suggest unpredictable ON–OFF. In such patients, the actual mechanism of wearing-off and peak-dose dyskinesia may reappear by increasing the levodopa intake interval to about 4 h. However, in some patients, the benefit may wane after weeks or months.

Dyskinesias

Peak-Dose Dyskinesia

- *Add amantadine* (**level A**) – most studies use 200 to 400 mg/day. The benefit may last <8 months. The use of other antiglutaminergic drugs is investigational.
- *Reduce individual levodopa dose size*, at the risk of increasing OFF time. The latter can be compensated for by increasing the number of daily doses of levodopa or increasing the doses of a dopamine agonist (**level C**).
- *Discontinue or reduce dose of MAO-B inhibitors or COMT inhibitors* (**good practice point**), at the risk of worsening wearing-off.
- *Add atypical antipsychotics*, clozapine (**level A**), with doses ranging between 12.5 and 75 mg/day up to 200 mg/day, or quetiapine (**level C**). However, clozapine is associated with potential serious adverse events (agranulocytosis and myocarditis), which limits its use (**good practice point**).
- *DBS of the STN*, which allows reduction of dopaminergic treatment (**level B**).
- *Apomorphine continuous subcutaneous infusion*, which allows reduction of levodopa therapy (**level C**).

Biphasic Dyskinesia

Biphasic dyskinesias can be very difficult to treat and have not been the subject of specific and adequate class I to III studies. Usually, the strategies described for peak-dose dyskinesias can also be considered for biphasic dyskinesia (**good practice point**). Another option is increasing the size and frequency of levodopa dose, at the risk of inducing or increasing peak-dose dyskinesia. This latter strategy can be helpful, generally transiently, in those cases without peak-dose dyskinesia, or where they are considered less disabling than the biphasic type. A further option could be larger, less frequent doses, to give a more predictable response, which would better enable patients to plan daily activities (**good practice point**).

Off-Period and Early Morning Dystonias

- *Usual strategies for wearing-off* can be applied in cases of off-period dystonia (**good practice point**).
- *Additional doses of levodopa or dopamine agonist therapy* at night may be effective for the control of dystonia appearing during the night or early in the morning (**good practice point**).
- *DBS of the STN* (**level B**).
- *Botulinum toxin* can be employed in both off-period and early morning dystonia (**good practice point**).

Freezing

Freezing, particularly freezing of gait, often occurs during the OFF phase and less frequently in both OFF and ON. The latter scenario often does not respond to dopaminergic strategies.

Options for OFF freezing are the same as those described for wearing-off. In addition, the use of visual or auditory cues is empirically useful for facilitating the start of the motor act once freezing has occurred (**level C**).

In ON freezing, trying a reduction in dopaminergic therapy is recommended, although this may result in worsening of wearing-off.

Neuropsychiatric Complications

Dementia

- *Discontinue potential aggravators*. Anticholinergics (**level B**), amantadine (**level C**), tricyclic antidepressants (**level C**), tolterodine and oxybutynin (**level C**) and benzodiazepines (**level C**).
- *Add cholinesterase inhibitors*. Rivastigmine (**level A**), donepezil (**level C**), galantamine (**level C**). Given the hepatotoxicity of tacrine, its use is not recommended (**good practice point**).

Psychosis

- *Control triggering factors* (**good practice point**). Treat infection and metabolic disorders, rectify fluid/electrolyte balance, treat sleep disorder.
- *Reduce polypharmacy* (**good practice point**). Reduce/stop anticholinergic antidepressants, reduce/stop anxiolytics/sedatives.
- Reduce antiparkinsonian drugs (**good practice point**). Stop anticholinergics, stop amantadine, reduce/stop dopamine agonists, reduce/stop MAO-B and COMT inhibitors, lastly, reduce levodopa. Stopping antiparkinsonian drugs can be at the cost of worsening motor symptoms.
- *Add atypical antipsychotics*. Clozapine (**level A**) – although it can be associated with serious haematological adverse events, requiring monitoring. There is insufficient data on quetiapine, but it is possibly useful (**good practice point**). Quetiapine is thought to be relatively safe and does not require blood monitoring. Olanzapine (**level A**) and risperidone (**level C**) are not recommended (harmful).
- *Typical antipsychotics* (e.g. phenothiazines, butyrophenones) should not be used because they worsen parkinsonism.
- *Add cholinesterase inhibitors*. Rivastigmine (**level B**), donepezil (**level C**). However, it must be noted that the cognitive improvements are only modest, whilst tremor worsened in some patients.

Depression

- Optimize antiparkinsonian therapy (**good practice point**).
- Tricyclic antidepressants (**good practice point**).
- SSRIs (**good practice point**). SSRI's are less probably to produce adverse effects than tricyclic antidepressants (**good practice point**).
- 'New' antidepressants – reboxetine, venlafaxine (no recommendation can be made).

Autonomic Dysfunction

Orthostatic Hypotension

- General measures:

    - *Avoid aggravating factors* such as large meals, alcohol, exposure to a warm environment and drugs known to cause orthostatic hypotension such as diuretics or antihypertensive drugs. Levodopa and dopamine agonists may also induce orthostatic hypotension.
    - *Increase salt intake* in symptomatic orthostatic hypotension.
    - *Head-up tilt of the bed at night*, which may be helpful.
    - *Wear elastic stockings*.
    - *Highlight postprandial effects*. In some patients, hypotension occurs only postprandially. Warning the patient about this effect and taking frequent small meals may be helpful.
- Drug therapy:
    - *Add midodrine* (**level A**).
    - *Add fludrocortisone* (**good practice point**: possibly effective, but note side-effects).

Urinary Disturbance

- *General measures for treating urinary urgency and incontinence*. Avoid coffee before bedtime, limit water ingestion before bedtime, etc.
- *Add peripherally acting anticholinergic drugs* (**good practice point**).
- *Add intranasal desmopressin spray* for nocturnal polyuria (insufficient evidence, no recommendation can be made).

Gastrointestinal Motility Problems

- *Apply general measures for treating constipation*. Diet, laxatives, etc.
- *Reduce or discontinue drugs with anticholinergic activity* (**good practice point**).
- *Add domperidone* (**level B**).

Erectile Dysfunction

- *Add sildenafil* (**level A**).
- *Add dopamine agonists*. Apomorphine and pergolide (insufficient evidence, no recommendation can be made).

Definitions:

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias

e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good practice points In cases where there is insufficient scientific evidence, a consensus statement ('good practice point') is made.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment of late Parkinson's disease

POTENTIAL HARMS

- *Monoamine oxidase isoenzyme type B (MAO-B) inhibitors*. Selegiline might increase or provoke dyskinesia in levodopa-treated patients, but this was not the primary outcome measure in the studies referred to. Rasagiline should not be added to selegiline because of cardiovascular safety issues.
- *Catechol-O-methyltransferase (COMT) inhibitors* should always be given with levodopa because of their mechanism of action. Tolcapone is potentially hepatotoxic, and is only recommended in patients failing on all other available medications.
- *Dopamine agonists*. When levodopa-treated patients with advanced Parkinson's disease receive a dopamine agonist to reduce OFF episodes, dyskinesia may occur or, if already present, worsen. In clinical practice, when an agonist is given as adjunct in patients with dyskinesias, the levodopa dose is usually reduced to minimize this problem. Nausea, headache, yawning and orthostatic hypotension are the most common side-effects of apomorphine. Pergolide and other ergot agonists are reserved for second-line treatment, because of their association with valvulopathy.
- *Clozapine* is associated with potential serious adverse events (agranulocytosis and myocarditis), which limits its use. Leucopenia is a rare (0.38%) but serious adverse event with clozapine. Consistently reported side-effects (even with low-dose clozapine) include sedation, dizziness, increased drooling, orthostatic hypotension, and weight gain.
- *Cholinesterase inhibitors* are associated with motor worsening, nausea, and vomiting.
- *Selective serotonin reuptake inhibitors (SSRIs)*. When added to dopaminergic therapy, SSRIs have the potential to induce a 'serotonin syndrome', which is a rare but serious adverse event.
- *Midodrine* is associated with supine hypertension.
- *Fludrocortisone*. Hypertension, hypokalaemia and ankle oedema are the main side effects of fludrocortisone.
- *Sildenafil*. Side-effects of this drug include a group of mild and transitory adverse reactions (headache, transient visual effects, flushing) and, occasionally, severe reactions (hypotension, priapism, cardiac arrest).

Refer to the National Guideline Clearinghouse (NGC) summary of the European Federation of Neurological Societies (EFNS) Part I guideline Early (uncomplicated) Parkinson's disease for more information on adverse effects of these and other antiparkinsonian drugs.

Deep brain stimulation (DBS) of the subthalamic nucleus (SSN) may cause adverse effects related to the *procedure* (i.e. acute confusion, intracerebral bleeding, stroke and seizures) or to *device dysfunction* (i.e. infection or stimulator repositioning, causing permanent severe morbidity or death). However, most adverse effects are related to the treatment (either stimulatory or stimulatory in combination with pharmacological treatment).

See the original guideline document for a more detailed explanation of adverse effects of DBS of the SSN.

CONTRAINDICATIONS

CONTRAINDICATIONS

For recommendations concerning drug dosage, method and route of administration, and contraindications, the reader is referred to the local formulary or the manufacturer's instruction except when provided within the guideline recommendations.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.
- For recommendations concerning drug dosage, method and route of administration, and contraindications the reader is referred to the local formulary or manufacturer's instruction, except when provided within the guidelines' recommendation itself.
- The opinions and views expressed in the paper are those of the authors and not necessarily those of the Movement Disorder Society (MDS) or its Scientific Issues Committee (SIC).

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Horstink M, Tolosa E, Bonuccelli U, Deuschl G, Friedman A, Kanovsky P, Larsen JP, Lees A, Oertel W, Poewe W, Rascol O, Sampaio C, European Federation of Neurological Societies, Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the EFNS and the MDS-ES. Part II: late (complicated) Parkinson's disease. Eur J Neurol 2006 Nov;13(11):1186-202. [196 references] PubMed

ADAPTATION

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

DATE RELEASED

2006 Nov

GUIDELINE DEVELOPER(S)

European Federation of Neurological Societies - Medical Specialty Society

SOURCE(S) OF FUNDING

European Federation of Neurological Societies

GUIDELINE COMMITTEE

European Federation of Neurological Societies and the Movement Disorder Society–European Section

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: M. Horstink, Department of Neurology, Radboud University Medical Centre, Nijmegen, The Netherlands; E. Tolosa, Neurology Service, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain; U. Bonuccelli, Department of Neurosciences, University of Pisa, Pisa, Italy; G. Deuschl, Department of Neurology, Christian-Albrechts-University Kiel, Germany; A. Friedman, Department of Neurology, Medical University of Warsaw, Warsaw, Poland; P. Kanovsky, Department of Neurology, Palacky University, Olomouc, Czech Republic; J. P. Larsen, Department of Neurology, Stavanger University Hospital, Stavanger, Norway; A. Lees, Reta Lila Weston Institute of Neurological Studies, London, UK; W. Oertel, Centre of Nervous Diseases, Philipps-University of Marburg, Marburg, Germany; W. Poewe, Department of Neurology, Innsbruck Medical University, Innsbruck, Austria; O. Rascol, Clinical Investigation Centre, Departments of Clinical Pharmacology and Neurosciences, University Hospital, Toulouse, France; C. Sampaio, Laboratorio de Farmacologia Clinica e Terapeutica e Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Lisbon, Portugal

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

M. Horstink has not received any departmental research grants or honoraria since starting this guidelines project.

E. Tolosa has received honoraria for research funding and consultancy from Novartis, Boehringer Ingelheim, Teva, Medtronic, Schwarz, and Servier.

U. Bonuccelli has acted as scientific advisor for, or obtained speaker honoraria from, Novartis, Boehringer Ingelheim, Pfizer, Chiesi, Schwarz, and GlaxoSmithKline. During the past 2 years he has received departmental grants and performed clinical studies for GlaxoSmithKline, Novartis, Teva, Chiesi, Boehringer, Schwarz, and Eisai.

G. Deuschl has acted as scientific advisor for, or obtained speaker honoraria from, Orina, Novartis, Boehringer Ingelheim, and Medtronic, during the past 2 years.

J.P. Larsen has received honoraria and research support from Orion Pharma and Pfizer, and has acted as a consultant for Lundbeck.

A. Lees has received honoraria for lectures from Novartis, Orion, Valeant, Britannia, GE-Amersham, Servier, Teva, GlaxoSmithKline, Boehringer Ingelheim, and Lundbeck.

W. Oertel has received honoraria for research funding and consultancy from Novartis, Boehringer Ingelheim, Schwarz, Medtronic, Teva, Orion, GlaxoSmithKline, Pfizer, and Solvay.

W. Poewe has received honoraria for lecturing and advisory board membership from Novartis, GlaxoSmithKline, Teva, Boehringer Ingelheim, Schwarz, and Orion.

O. Rascol has received honoraria for research funding and/or consultancy from GlaxoSmithKline, Novartis, Boehringer Ingelheim, Eli Lilly, Teva, Lundbeck, Schwarz, and Servier.

C. Sampaio has received departmental research grants from Novartis Portugal. Her department has also charged consultancy fees to Servier and Lundbeck, and she has received honoraria for lectures from Boehringer Ingelheim.

A. Friedman and P. Kanovsky have nothing to declare.

GUIDELINE STATUS

This is the current release of the guideline.

The guidelines will need to be updated no later than 2009.

GUIDELINE AVAILABILITY

Electronic copies: Available to registered users from the European Federation of Neurological Societies Web site.

Print copies: Available from Dr M. W. I. M. Horstink, Department of Neurology, Radboud University Medical Centre, Nijmegen, the Netherlands; Phone: +31-24-3615202; Fax +31-24-3541122; E-mail: m.horstink@neuro.umcn.nl

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site.
- Guideline papers. European Federation of Neurological Societies. Electronic copies: Available from the European Federation of Neurological Societies Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 12, 2007. The information was verified by the guideline developer on May 15, 2007. This summary was updated by ECRI Institute on November 6, 2007, following the updated U.S. Food and Drug Administration advisory on Viagra, Cialis, Levitra, and Revatio. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on December 7, 2007, following the U.S. Food and Drug Administration advisory on Desmopressin Acetate. This summary was updated by ECRI Institute on July 25, 2008, following the U.S. Food and Drug Administration advisory on Antipsychotics.

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