



Complete Summary

GUIDELINE TITLE

European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society.

BIBLIOGRAPHIC SOURCE(S)

Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. *J Peripher Nerv Syst* 2006 Mar;11(1):1-8. [59 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

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

- [September 11, 2008, Rituxan \(Rituximab\)](#): Genentech informed healthcare professionals of revisions to prescribing information for Rituxan regarding a case of progressive multifocal leukoencephalopathy (PML) leading to death in a patient with rheumatoid arthritis who received Rituxan in a long-term safety extension clinical study.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

SCOPE

DISEASE/CONDITION(S)

Multifocal motor neuropathy (MMN)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To construct guidelines for the definition, diagnosis, and treatment of multifocal motor neuropathy (MMN) based on the available evidence and, where adequate evidence was not available, consensus

TARGET POPULATION

Patients presenting with multifocal motor neuropathy (MMN)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Clinical examination
2. Electrodiagnostic tests
3. Anti-ganglioside GM1 antibody testing
4. Magnetic resonance imaging (MRI) of the brachial plexus
5. Cerebrospinal fluid (CSF) examination
6. Investigations for concomitant disease or to exclude other possible causes

Treatment

1. Intravenous immunoglobulin (IVIg) as the first line of treatment

2. Repeated IVIg treatment if effective
3. Cyclosporine, azathioprine, interferon-beta 1a (IFN-beta 1a), cyclophosphamide, or rituximab if IVIg is not effective

MAJOR OUTCOMES CONSIDERED

- Muscle strength
- Numbers of conduction blocks (CBs)
- Axonal degeneration

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Task Force searched MEDLINE from 1980 onwards to July 24, 2004 for articles on multifocal motor neuropathy (MMN) and "diagnosis" or "treatment" or "guideline" but found that the personal databases of Task Force members were more useful. They also searched the Cochrane Library in September 2004.

NUMBER OF SOURCE DOCUMENTS

More than 400 documents were retrieved during the literature search.

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 Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

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

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This guideline has been produced by the Task Force members of the European Federation of Neurological Societies (EFNS) who are also members of the Peripheral Nerve Society (PNS). Additional non-European members of the Task

Force were appointed on the recommendation of the Board of Directors of the PNS.

Methods for Reaching Consensus

Pairs of Task Force members prepared draft statements about definition, diagnosis, and treatment, which were considered at a meeting in September 2004. Evidence was classified as class I to IV and recommendations as level A to C according to the scheme agreed for EFNS guidelines (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields). When only class IV evidence was available but consensus could be reached, the Task Force offered advice as good practice points. The statements were revised and collated into a single document, which was then revised iteratively until consensus was reached.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

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 Point (GPP) When only class IV evidence was available but consensus could be reached, the Task Force offered advice as good practice points.

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (Hughes RAC, Barnes MP, Baron J, Brainin M [2001]. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces. *Eur J Neurol* 8:549-550).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good Practice Point [GPP]) are defined at the end of the "Major Recommendations" field.

Diagnostic Criteria (Good Practice Points)

1. Clinical: the two core criteria and all exclusion criteria should be met (see Table 1, below)
2. Electrodiagnostic: definite or probable conduction block (CB) in at least two nerves (see Table 2, below)
3. Supportive: anti-GM1 antibody testing, magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) examination, and treatment response (see Table 3, below)
4. Categories: definite and probable multifocal motor neuropathy (MMN) (see Table 4, below)

Table 1. Clinical Criteria for Multifocal Motor Neuropathy (MMN)
Core criteria (both must be present)
<ol style="list-style-type: none">1. Slowly progressive or stepwise progressive, asymmetric limb weakness, or motor involvement having a motor nerve distribution in at least two nerves, for more than 1 month*2. No objective sensory abnormalities except for minor vibration sense abnormalities in the lower limbs
Supportive clinical criteria
<ol style="list-style-type: none">3. Predominant upper limb involvement**4. Decreased or absent tendon reflexes in the affected limb***5. Absence of cranial nerve involvement^6. Cramps and fasciculations in the affected limb

Exclusion criteria

- 7. Upper motor neuron signs
- 8. Marked bulbar involvement
- 9. Sensory impairment more marked than minor vibration loss in the lower limbs
- 10. Diffuse symmetric weakness during the initial weeks
- 11. Laboratory: cerebrospinal fluid protein >1g/L

*Usually more than 6 months.

**At onset, predominant lower limb involvement accounts for nearly 10% of the cases.

***Slightly increased tendon reflexes, in particular in the affected arm, have been reported and do not exclude the diagnosis of MMN provided criterion 7 is met.

^12th nerve palsy has been reported.

Table 2. Electrophysiological Criteria for Conduction Block (CB)* (Good Practice Points)

- 1. Definite motor CB*
Negative compound muscle action potential (CMAP) area reduction on proximal versus distal stimulation of at least 50% whatever the nerve segment length (median, ulnar, and peroneal). Negative CMAP amplitude on stimulation of the distal part of the segment with motor CB must be >20% of the lower limit of normal and >1mV (baseline negative peak) and an increase of proximal negative peak CMAP duration must be ≤30%.
- 2. Probable motor CB*
Negative CMAP area reduction of at least 30% over a long segment of an upper limb nerve with an increase of proximal negative peak CMAP duration ≤30%, *or*
Negative CMAP area reduction of at least 50% (same as definite) with an increase of proximal negative peak CMAP duration >30%
- 3. Normal sensory nerve conduction in upper limb segments with CB and normal sensory nerve action potential (SNAP) amplitudes (see exclusion criteria)

*Evidence for CB must be found at sites distinct from common entrapment or compression syndromes.

Table 3. Supportive Criteria

- 1. Elevated immunoglobulin M anti-ganglioside GM1 antibodies (**level A recommendation**)
- 2. Magnetic resonance imaging showing gadolinium enhancement and/or hypertrophy of the brachial plexuses (**good practice point**)
- 3. Clinical improvement following intravenous immunoglobulin treatment (**good practice point**)

Table 4. Diagnostic Categories

<p>Definite MMN</p> <p>Clinical criteria 1, 2, and 7 to 11 and electrophysiological criteria 1 and 3 in one nerve</p>
<p>Probable MMN</p> <p>Clinical criteria 1, 2, and 7 to 11 and electrophysiological criteria 2 and 3 in two nerves</p> <p>Clinical criteria 1, 2, and 7 to 11 and electrophysiological criteria 2 and 3 in one nerve and at least one supportive criterion 1 to 3 (see Table 3 above)</p>

Diagnostic Tests (Good Practice Points)

1. Clinical examination and electrodiagnostic tests should be considered in all patients.
2. Anti-ganglioside GM1 antibody testing, MRI of the brachial plexus, and CSF examination should be considered in selected patients.
3. Investigations to discover concomitant disease or exclude other possible causes should be considered, but the choice of tests will depend on the individual circumstances.

Treatment

1. Intravenous immunoglobulin (IVIg) (2 g/kg given over 2 to 5 days) should be considered as the first line of treatment (**level A recommendation**) when disability is sufficiently severe to warrant treatment
2. Corticosteroids are not recommended (**good practice point**)
3. If an initial treatment with IVIg is effective, repeated IVIg treatment should be considered in selected patients (**level C recommendation**). The frequency of IVIg maintenance therapy should be guided by the response (**good practice point**). Typical treatment regimen is 1 g/kg every 2 to 4 weeks or 2 g/kg every 1 to 2 months (**good practice point**)
4. If IVIg is not (or not sufficiently) effective, then immunosuppressive treatment may be considered. Cyclophosphamide, cyclosporine, azathioprine, interferon-beta 1a (IFNβ1a), or rituximab are possible agents (**good practice point**)
5. Toxicity makes cyclophosphamide a less desirable option (**good practice point**).

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons

with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

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 for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

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 Point (GPP) When only class IV evidence was available but consensus could be reached, the Task Force offered advice as good practice points.

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 diagnosis and treatment of multifocal motor neuropathy (MMN) resulting in improved disability

POTENTIAL HARMS

- Cyclophosphamide is associated with toxicity which makes it less desirable option than other immunosuppressants.
- Patients taking interferon beta-1a have been reported rarely to experience severe hepatic injury, including cases of hepatic failure.

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. This guideline is not intended to have implications regarding reimbursement.

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.

IMPLEMENTATION TOOLS

Staff Training/Competency Material

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

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst 2006 Mar;11(1):1-8. [59 references] [PubMed](#)

ADAPTATION

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

DATE RELEASED

2006 Mar

GUIDELINE DEVELOPER(S)

European Federation of Neurological Societies - Medical Specialty Society
Peripheral Nerve Society - Disease Specific Society

SOURCE(S) OF FUNDING

European Federation of Neurological Societies

GUIDELINE COMMITTEE

Joint Task Force European Federation of Neurological Societies and the Peripheral Nerve Society

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: Ivo N. van Schaik, Netherlands; Pierre Bouche, France; Isabel Illa, Spain; Jean- Marc Leger, France; Peter Van den Bergh, Belgium; David R. Cornblath, USA; Eileen Evers, UK; Robert D. Hadden, UK; Richard A. C. Hughes (*Chair*), UK; Carol L. Koski, USA; Eduardo Nobile-Orazio, Italy; John D. Pollard, Australia; Claudia Sommer, Germany; Pieter A. van Doorn, Netherlands

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The following authors have reported conflicts of interest:

R. Hughes, personal none, departmental research grants or honoraria from Bayer, Biogen-Idec, Schering-Laboratoire Francais du Biofractionnement (LFB), and Kedrion

D. Cornblath, personal honoraria from Aventis Behring and Baxter

C. Koski, personal honoraria from American Red Cross, Baxter, Bayer, and ZLB-Behring

J. M. Leger, personal none, departmental research grants or honoraria from Biogen-Idec, Baxter, LFB, and Octapharma

E. Nobile-Orazio, personal honoraria from Kedrion, Grifols, Baxter, and LFB (and he has been commissioned by Kedrion and Baxter to give expert opinions to the Italian Ministry of Health on the use of IVIg in dysimmune neuropathies)

J. Pollard, personal none, departmental research grants from Biogen-Idec and Schering

P. van Doorn, personal none, departmental research grants or honoraria from Baxter and Bayer

The other authors have nothing to declare.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available to registered users from the [European Federation of Neurological Societies Web site](#).

Print copies: Available from Richard A. C. Hughes, Department of Clinical Neuroscience, King's College London School of Medicine, Guy's Hospital, London SE1 1UL, UK; E-mail: richard.a.hughes@kcl.ac.uk

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](#).
- Continuing Medical Education questions available from the [European Journal of Neurology Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on December 8, 2006. The information was verified by the guideline developer on January 2, 2007. This summary was updated by ECRI Institute on May 17, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Gadolinium-based contrast agents. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on October 8, 2008 following the U.S. Food and Drug Administration advisory on Rituxan (rituximab).

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the Blackwell-Synergy copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 11/3/2008

