# Complete Summary

## GUIDELINE TITLE

Evidence report: the medical treatment of ocular myasthenia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology.

## BIBLIOGRAPHIC SOURCE(S)

Benatar M, Kaminski HJ, Quality Standards Subcommittee of the American Academy of Neurology. Evidence report: the medical treatment of ocular myasthenia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2007 Jun 12;68(24):2144-9. [20 references]

## GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

Ocular myasthenia

### GUIDELINE CATEGORY

Management
Treatment

### CLINICAL SPECIALTY

Neurology
Ophthalmology

### INTENDED USERS

Physicians

### GUIDELINE OBJECTIVE(S)

- To perform a systematic review of the relevant literature and to provide evidence-based guidelines for the medical treatment of ocular myasthenia
- To address two specific questions: 1) Does pharmacologic treatment lead to an improvement in ocular symptoms (diplopia and ptosis)? and 2) Is pharmacologic treatment associated with a reduced risk of progression from ocular to generalized myasthenia gravis (MG)?

### TARGET POPULATION

Patients presenting with ocular myasthenia

### INTERVENTIONS AND PRACTICES CONSIDERED

Corticosteroids and/or azathioprine were considered but could not be recommended because of the absence of evidence

### MAJOR OUTCOMES CONSIDERED

Effectiveness of therapy

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

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

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Two neurologists with experience in the evaluation and treatment of patients with myasthenia gravis (MG) were appointed by the American Academy of Neurology Quality Standards Subcommittee to prepare this review. The Cochrane Neuromuscular Disease Group Register was searched for randomized controlled trials; Medline (1966 to 2004) and EMBASE (1980 to 2004) were also searched for randomized controlled trials, case–control studies, and cohort studies. Search terms included *myasthenia gravis*, *eye*, *ocular*, and *vision*, as well as a series of terms describing specific therapies and specific types of clinical studies. To be included in the review, studies had to meet three criteria: 1) randomized (or quasi-randomized) controlled trial or observational (cohort or case– control) study design; 2) active treatment compared with placebo, no treatment, or some other treatment; and 3) results reported separately for patients with ocular myasthenia

(Grade 1) as defined by the Myasthenia Gravis Foundation of America. Studies reporting outcome in children and adults were considered.

## NUMBER OF SOURCE DOCUMENTS

Two randomized controlled trials (RCTs) and five observational studies were identified.

## 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

### Classification of Therapeutic Evidence

**Class I**: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required: a) primary outcome(s) clearly defined; b) exclusion/inclusion criteria clearly defined; c) adequate accounting for dropouts and cross-overs with numbers sufficiently low to have minimal potential for bias; d) 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–d above OR a randomized controlled trial (RCT) in a representative population that lacks one criteria a–d.

**Class III**: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.*

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

*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

## METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The quality of randomized controlled trials was evaluated in six domains—method of randomization, allocation concealment, patient blinding, observer blinding, explicit inclusion/exclusion criteria, and completeness of follow-up—using a set of predefined criteria. The quality of observational studies was similarly evaluated in

three domains—control for confounding, completeness of follow-up, and observer blinding—using predefined criteria. The method of randomization was graded as adequate (computer-generated random numbers, tables of random numbers, coin toss), unclear (statement made that trial is randomized but method not described), or inadequate (quasi-randomized).

Allocation concealment was graded as adequate (identical prenumbered containers prepared by an independent pharmacy of central randomization unit or sequentially numbered opaque sealed envelopes), unclear (no details given of how the next assignment in the sequence was concealed), inadequate (open allocation schedule, unsealed or nonopaque envelopes, alternation, days of week, etc.), or not done. Patient and observer blinding were graded as adequate (method of blinding described and thought to be sufficient to ensure that the investigator was unaware of the treatment received at the time outcome evaluation was performed), unclear (authors state that study was blinded, but details not provided), inadequate (some method used to blind investigators, but technique was unreliable), or not done. Completeness of follow-up was graded as adequate (analysis performed with >80% of patients), unclear (insufficient details provided on withdrawals, dropouts, etc.), inadequate (<80% of patients included in the analysis), or not done. Finally, control for confounding was graded as adequate (multivariate analysis that included at least two factors—age, duration of ocular symptoms before initiation period of follow-up, concomitant immunosuppressive therapy, duration of follow-up after entry into the study, antibody status, presence of abnormalities on repetitive nerve stimulation or single fiber electromyography—or data presented showing that the treatment groups were comparable at baseline with respect to this same set of factors), unclear (authors state that they controlled for confounding, but details not given), inadequate (some effort made to control for confounding, but insufficient number of relevant factors were considered in the analysis), or not done.

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

### Classification of Recommendations

**A** = Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)

**B** = Probably effective, ineffective, or harmful for the given condition in the specified population. (Level B rating requires at least one Class I study or at least two consistent Class II studies.)

**C** = Possibly effective, ineffective, or harmful for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

**U** = Data inadequate or conflicting; given current knowledge, treatment is unproven.

### COST ANALYSIS

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

### METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Drafts of the guideline have been reviewed by at least three American Academy of Neurology (AAN) committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields.

The guideline was approved by the Quality Standards Subcommittee on July 29, 2006; by the Practice Committee on March 15, 2007; and by the American Academy of neurology Board of Directors on April 5, 2007.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Definitions of the classification of therapeutic evidence (Class I–IV), and strength of recommendations (A, B, C, U) are provided at the end of the "Major Recommendations" field.

**Are Cholinesterase Inhibitors, Corticosteroids, or Other Immunosuppressive Agents Effective in Improving Visual Symptoms in Ocular Myasthenia?**

*Recommendations*

Given the absence of evidence, it is not possible to make any evidence-based recommendations regarding the effects of cholinesterase inhibitors, corticosteroids, or other immunosuppressive agents in improving the symptoms of ocular myasthenia.

**Are Cholinesterase Inhibitors, Corticosteroids, or Other Immunosuppressive Agents Effective in Reducing the Risk of Progression from Ocular to Generalized Myasthenia Gravis (MG)?**

*Recommendations*

For patients with ocular myasthenia, the evidence does not support or refute the use of corticosteroids and/or azathioprine to reduce the risk of progression to generalized MG (**Level U**). The decision to use such agents should be weighed against the potential for harmful side effects of these medications. Furthermore, it is not possible to make any evidence-based recommendations with regard to the question of whether cholinesterase inhibitors have any effect in reducing the risk of progression to generalized MG. Recommendations cannot be made because of an absence of evidence.

**Definitions**:

**Classification of Therapeutic Evidence**

**Class I**: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required: a) primary outcome(s) clearly defined; b) exclusion/inclusion criteria clearly defined; c) adequate accounting for dropouts and cross-overs with numbers sufficiently low to have minimal potential for bias; d) 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–d above OR a randomized controlled trial (RCT) in a representative population that lacks one criteria a–d.

**Class III**: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.*

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

*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

**Classification of Recommendations**

**A** = Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)

**B** = Probably effective, ineffective, or harmful for the given condition in the specified population. (Level B rating requires at least one Class I study or at least two consistent Class II studies.)

**C** = Possibly effective, ineffective, or harmful for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

**U** = Data inadequate or conflicting; given current knowledge, treatment is unproven.

### 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 each recommendation (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate treatment of ocular myasthenia

### POTENTIAL HARMS

Not stated

## QUALIFYING STATEMENTS

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- This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.
- The absence of high-quality evidence means that it is not possible to make any evidence-based recommendations regarding the effects of cholinesterase inhibitors, corticosteroids, or other immunosuppressive agents with respect to improvement of ocular symptoms. There is similarly an absence of evidence regarding the effects of cholinesterase inhibitors on the risk of progression to generalized myasthenia gravis (MG).

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## 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)

Benatar M, Kaminski HJ, Quality Standards Subcommittee of the American Academy of Neurology. Evidence report: the medical treatment of ocular myasthenia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2007 Jun 12;68(24):2144-9. [20 references]

### ADAPTATION

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

### DATE RELEASED

2007 Jun 12

### GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society

### SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

### GUIDELINE COMMITTEE

Quality Standards Subcommittee

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The American Academy of Neurology (AAN) is committed to producing independent, critical and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least three AAN committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com. With regards to this specific report, all authors have stated that they have nothing to disclose.

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the American Academy of Neurology Web site.

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI Institute on October 9, 2007.

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