



## Complete Summary

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### GUIDELINE TITLE

Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient.

### BIBLIOGRAPHIC SOURCE(S)

Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient. Am J Health Syst Pharm 2002 Jan 15;59(2):179-95. [78 references] [PubMed](#)

Neuromuscular Blockade Task Force. Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient. Crit Care Med 2002;30(1):142-56. [78 references] [PubMed](#)

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## SCOPE

### DISEASE/CONDITION(S)

Conditions in the critically ill or injured adult for which neuromuscular blockade is indicated, including:

- Conditions requiring mechanical ventilation (e.g., respiratory failure)
- Muscle spasms associated with tetanus
- Increased intracranial pressure
- Decreased oxygen consumption

### GUIDELINE CATEGORY

Management  
Treatment

## CLINICAL SPECIALTY

Anesthesiology  
Critical Care  
Neurology  
Nursing  
Pharmacology  
Pulmonary Medicine

## INTENDED USERS

Advanced Practice Nurses  
Nurses  
Pharmacists  
Physician Assistants  
Physicians

## GUIDELINE OBJECTIVE(S)

To update the 1995 Society of Critical Care Medicine recommendations for the use of neuromuscular blocking agents (NMBAs) in the intensive care unit (ICU)

## TARGET POPULATION

Critically ill adults

## INTERVENTIONS AND PRACTICES CONSIDERED

1. Treatment with nondepolarizing neuromuscular blocking agents (NMBAs):
  - Aminosteroidal compounds, including pancuronium, pipecuronium, vecuronium, rocuronium, and rapacuronium (Note: rapacuronium has been withdrawn from the U.S. market because of reports of morbidity and mortality associated with its use.)
  - Benzylisoquinolinium compounds including D-tubocurarine, atracurium, cisatracurium, doxacurium, mivacurium
2. Monitoring depth of neuromuscular blockade via visual, tactile, or electronic assessment of patient's muscle tone (e.g., train-of-four monitoring, clinical assessment)
3. Use of sedative and analgesic drugs prior to initiating neuromuscular blockade

## MAJOR OUTCOMES CONSIDERED

- Depth of neuromuscular blockade
- Pharmacokinetics (volume of distribution, elimination half-life, metabolic clearance rate) of neuromuscular blocking agents
- Median time to recovery
- Intracranial pressure, cerebral perfusion pressure, cerebral blood flow
- Changes in hemodynamic parameters (e.g., blood pressure, heart rate)
- Muscle spasms associated with tetanus
- Oxygen consumption, oxygen delivery, oxygen extraction ratios, and gastric intramucosal pH

- Adverse effects of neuromuscular blockade

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

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

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

A comprehensive literature search was performed to develop the clinical practice guideline. Published studies identified through a MEDLINE search (Neuromuscular blocking agents 1994-2001) were reviewed, as were the reference lists of the retrieved documents and abstracts from meetings of professional associations. The literature was critically evaluated for research design, patient selection, medication dose, administration route, combination treatment, test measures, statistics, and results.

### 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

Categories (Levels) of Literature Evaluation:

1. Results from a single prospective, randomized, controlled trial or from a meta-analysis of prospective, randomized, controlled trials
2. Results from a single prospective, randomized, controlled trial or from a meta-analysis of prospective, randomized, controlled trials, in which the confidence interval for the treatment effect overlaps the minimal clinically important benefit
3. Results from nonrandomized, concurrent, cohort studies
4. Results from nonrandomized, historical, cohort studies
5. Results from case studies
6. Recommendations based on expert opinion

### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The medical literature ranged in quality from prospective randomized trials and retrospective observations to expert opinions. After the authors identified and classified their respective studies, they graded the articles on the basis of the results of the review. Pertinent references were assigned a score to account for variance in quality. The recommendations of the Society of Critical Care Medicine, American College of Critical Care Medicine, and the American Society of Health-System Pharmacists (Joint Task Force) were graded according to the strength and quality of the scientific evidence. A substantial effort was made by the Joint Task Force to adhere to the methodology for developing a scientifically sound clinical practice guideline as prescribed by the American Medical Association, the Institute of Medicine, and the Canadian Medical Association.

#### METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations:

- A. Methods strong, results consistent, prospective, randomized, controlled trials, no heterogeneity
- B. Methods strong, results inconsistent, prospective, randomized, controlled trials, heterogeneity present
- C. Methods weak, observational studies

#### COST ANALYSIS

There have been few formal pharmacoeconomic evaluations of neuromuscular blocking agents (NMBAs). In one of these economic evaluations, medication-related cost savings were found when voluntary prescribing guidelines for NMBAs were initiated in the operating room of a university hospital. In another study that involved randomization to one of three NMBAs, there were no significant cost differences between atracurium, vecuronium, and rocuronium for surgeries lasting two hours or less, but vecuronium and rocuronium were economically advantageous if the duration of surgery was two to four hours. In a third retrospective study, long-acting NMBAs (e.g., D-tubocurarine and pancuronium) were associated with prolonged postoperative recovery compared with shorter-acting agents (e.g., atracurium, mivacurium, and vecuronium). The authors noted in the discussion section of the paper that based on intrainstitutional recovery room costs, delays in recovery times seen with the longer-acting agents offset the expected savings in drug costs. For patients transferred to the intensive care unit (ICU), this may not be a major problem.

Two pharmacoeconomic investigations involving NMBAs in the ICU evaluated the costs associated with prolonged recovery following discontinuation of nondepolarizing NMBAs. In one study, overall costs were lower when Train-of-four (TOF) monitoring was employed. In another study, patients who had prolonged motor weakness after discontinuing NMBAs were compared with a control group; ICU and hospital costs were substantially higher in the patients with prolonged weakness.

A study involving 40 academic medical centers with patients undergoing coronary artery bypass graft surgery found no significant differences in duration of intubation or duration of ICU or hospital stay among patients who received pancuronium (n = 732), vecuronium (n = 130), or both (n = 242) agents. It is unknown if these results pertain to subgroups of patients, such as those with renal or hepatic dysfunction. If the results of this study are confirmed, the choice of agent could be based solely on cost minimization using medication purchase cost information and equipotent dosage regimens.

A prospective, randomized trial comparing TOF to standard clinical assessment showed decreased NMBA usage and faster return of spontaneous ventilation with TOF monitoring. TOF has the potential to decrease costs associated with NMBA use in ICUs.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The following professional organizations reviewed the guideline: the American College of Chest Physicians, the American Academy of Neurology, the American Association of Critical Care Nurses, the American Nurses Association, the American Pharmaceutical Association, and the American College of Clinical Pharmacy. In addition, ten individuals are acknowledged in the original guideline document for their review efforts.

# RECOMMENDATIONS

## MAJOR RECOMMENDATIONS

The grades of recommendations (A-C) are defined at the end of the "Major Recommendations" field.

1. Neuromuscular blocking agents (NMBAs) should be used for an adult patient in an intensive care unit (ICU) to manage ventilation, manage increased intracranial pressure (ICP), treat muscle spasms, and decrease oxygen consumption only when all other means have been tried without success. (Grade of recommendation = C)
2. The majority of patients in an intensive care unit who are prescribed a neuromuscular blocking agent can be managed effectively with pancuronium. (Grade of recommendation = B)
3. For patients for whom vagolysis is contraindicated (e.g., those with cardiovascular disease), neuromuscular blocking agents other than pancuronium may be used. (Grade of recommendation = C)
4. Because of their unique metabolism, cisatracurium or atracurium is recommended for patients with significant hepatic or renal disease. (Grade of recommendation = B)
5. Patients receiving neuromuscular blocking agents should be assessed both clinically and by train-of-four monitoring (Grade of recommendation = B),

- with a goal of adjusting the degree of neuromuscular blockade to achieve one or two twitches. (Grade of recommendation = C)
6. Before initiating neuromuscular blockade, patients should be medicated with sedative and analgesic drugs to provide adequate sedation and analgesia in accordance with the physician's clinical judgment to optimize therapy. (Grade of recommendation = C)
  7. For patients receiving neuromuscular blocking agents and corticosteroids, every effort should be made to discontinue neuromuscular blocking agents as soon as possible. (Grade of recommendation = C)
  8. Drug holidays (i.e., stopping neuromuscular blocking agents daily until forced to restart them based on the patient's condition) may decrease the incidence of acute quadriplegic myopathy syndrome (AQMS). (Grade of recommendation = C)
  9. Patients receiving neuromuscular blocking agents should have prophylactic eye care (Grade of recommendation = B), physical therapy (Grade of recommendation = C), and deep vein thrombosis prophylaxis (DVT). (Grade of recommendation = C)
  10. Patients who develop tachyphylaxis to one neuromuscular blocking agent should try another drug if neuromuscular blockade is still required. (Grade of recommendation = C)
  11. Institutions should perform an economic analysis using their own data when choosing neuromuscular blocking agents for use in an intensive care unit. (Grade of recommendation = C)

#### Definitions:

#### Grades of Recommendations:

- A. Methods strong, results consistent, prospective, randomized, controlled trials, no heterogeneity
- B. Methods strong, results inconsistent, prospective, randomized, controlled trials, heterogeneity present
- C. Methods weak, observational studies

#### CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for the use of neuromuscular blocking agents in the intensive care unit.

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field). The medical literature ranged in quality from prospective randomized trials and retrospective observations to expert opinions.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate and safe use of neuromuscular blockade in the critically ill or injured patient

### POTENTIAL HARMS

General complications associated with neuromuscular blocking agents in the intensive care unit include:

- Awake, paralyzed patient-anxiety and panic
- Risk of ventilator disconnect or airway mishap
- Autonomic and cardiovascular effects (i.e., vagolytic)
- Decreased lymphatic flow
- Risk of generalized deconditioning
- Skin breakdown
- Peripheral nerve injury
- Corneal abrasion, conjunctivitis
- Myositis ossificans
- Risk of prolonged muscle weakness, acute quadriplegic syndrome (AQMS)
- Potential central nervous system toxicity

Specific complications of neuromuscular-blocking agents:

#### Vecuronium

- Vecuronium has been reported to be more commonly associated with prolonged blockade once discontinued, compared with other neuromuscular blocking agents.
- Patients receiving vecuronium and corticosteroids were at increased risk of prolonged weakness once the drug was discontinued.

#### D-tubocurarine

- D-tubocurarine induces histamine release and autonomic ganglion blockade. Hypotension is rare, however, when the agent is administered slowly in appropriate dosages.

#### Atracurium

- Atracurium has minimal cardiovascular adverse effects and is associated with histamine release at higher doses.
- Laudanosine is a breakdown product of Hofmann elimination of atracurium and has been associated with central nervous system excitation. This has led to concern about the possibility of precipitating seizures in patients who have received extremely high doses of atracurium or who are in hepatic failure. Long-term infusions have been associated with the development of tolerance, necessitating significant dose increases or conversion to other neuromuscular

blocking agents. Atracurium has been associated with persistent neuromuscular weakness as have other neuromuscular blocking agents.

#### Cisatracurium

- Prolonged weakness has been reported following the use of cisatracurium.

#### Pancuronium

- The two adverse effects of pancuronium that are commented on frequently are vagolysis and an increase in heart rate

Note: A number of drugs interact with neuromuscular blocking agents and can either potentiate or antagonize their action. These drugs are listed in Table 7 titled "Drug-drug Interactions of Neuromuscular Blocking Agents (NMBAs)" in the original guideline document.

#### Subgroups Most Likely to be Harmed:

- Pancuronium is vagolytic, which limits its use in patients who cannot tolerate an increase in heart rate (e.g., patients with cardiovascular disease).
- In elderly patients and patients with renal dysfunction, a significant prolongation of effect may occur with doxacurium.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- The clinical practice guideline issued for 2002 is comprehensive and based on available evidence. This field is still constrained by a dearth of high-quality, randomized prospective trials comparing agents, monitoring techniques, and scoring scales.
- These recommendations in these documents may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on professional judgment, level of care, individual patient circumstances, and available resources.

## 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

## IOM DOMAIN

Effectiveness  
Safety

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient. Am J Health Syst Pharm 2002 Jan 15;59(2):179-95. [78 references] [PubMed](#)

Neuromuscular Blockade Task Force. Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient. Crit Care Med 2002;30(1):142-56. [78 references] [PubMed](#)

### ADAPTATION

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

### DATE RELEASED

1995 (revised 2002)

### GUIDELINE DEVELOPER(S)

American College of Critical Care Medicine - Professional Association  
American Society of Health-System Pharmacists - Professional Association  
Society of Critical Care Medicine - Professional Association

### SOURCE(S) OF FUNDING

Society of Critical Care Medicine (SCCM)

American Society of Health-System Pharmacists (ASHP)

### GUIDELINE COMMITTEE

Neuromuscular Blockade Task Force

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Neuromuscular Blockade Task Force Members: Michael J. Murray, M.D., Ph.D., FCCM (Chair); Jay Cowen, M.D.; Heidi F. DeBlock, M.D.; Brian L. Erstad, Pharm.D., FCCM; Anthony W. Gray, Jr., M.D., FCCM; Judith Jacobi, Pharm.D., FCCM, BCPS; Philip D. Lumb, M.B., B.S., FCCM; William T. McGee, M.D., M.H.A.; Stanley A. Nasraway, Jr, M.D., FCCM; William T. Peruzzi, M.D., FCCM; Richard C. Prielipp, M.D., FCCM; Greg Susla, Pharm.D., FCCM; Ann N. Tescher, R.N.

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## ENDORSER(S)

American College of Chest Physicians - Medical Specialty Society

## GUIDELINE STATUS

This is the current release of the guideline. It updates a previously issued version (Practice parameters for sustained neuromuscular blockade in the adult critically ill patient: an executive summary. Society of Critical Care Medicine; Crit Care Med 1995 Sep;23[9]:1601-5).

An update is not in progress at this time.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Society of Critical Care Medicine \(SCCM\) Web site](#). Also available from the [American Society of Health-System Pharmacists \(ASHP\) Web site](#).

Print copies: Available from SCCM, 701 Lee Street, Suite 200, Des Plaines, IL 60016; Telephone: (847) 827-6869; Fax: (847) 827-6886; On-line through the [SCCM Bookstore](#).

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Sedation, analgesia, and neuromuscular blockade of the critically ill adult: revised clinical practice guidelines for 2002. Crit Care Med 2002 Jan;30(1):117-8; also published in Am J Health Syst Pharm 2002 Jan 15;59(2):147-9.

Electronic copies: Available from the [American Society of Health-System Pharmacists \(ASHP\) Web site](#).

Print copies: Available from SCCM, 701 Lee Street, Suite 200, Des Plaines, IL 60016; Telephone: (847) 827-6869; Fax: (847) 827-6886; On-line through the [SCCM Bookstore](#).

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on July 22, 2002. The information was verified by the guideline developers on August 1, 2002.

#### COPYRIGHT STATEMENT

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Date Modified: 11/15/2004

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