



## Complete Summary

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### GUIDELINE TITLE

EFNS guideline on the management of status epilepticus.

### BIBLIOGRAPHIC SOURCE(S)

Meierkord H, Boon P, Engelsen B, Gocke K, Shorvon S, Tinuper P, Holtkamp M. EFNS guideline on the management of status epilepticus. Eur J Neurol 2006 May;13(5):445-50. [40 references] [PubMed](#)

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

- Generalised convulsive status epilepticus (GCSE)
- Non-convulsive status epilepticus (NCSE)

**Note:** The following conditions are not considered in this guideline:

- Post-anoxic myoclonus
- Status epilepticus in children

### GUIDELINE CATEGORY

Management  
Treatment

## **CLINICAL SPECIALTY**

Anesthesiology  
Emergency Medicine  
Family Practice  
Internal Medicine  
Neurology

## **INTENDED USERS**

Emergency Medical Technicians/Paramedics  
Physicians

## **GUIDELINE OBJECTIVE(S)**

- To review the literature and discuss the degree of evidence for various treatment strategies for generalised convulsive (GCSE) and non-convulsive status epilepticus (NCSE)
- To summarise published treatment options for GCSE and NCSE

## **TARGET POPULATION**

Adults with generalized convulsive and non-convulsive status epilepticus in critical care situations

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Management/Treatment**

1. Initial management:
  - Assessment and control of airways and ventilation
  - Arterial blood gas monitoring
  - Electrocardiogram (ECG)
  - Blood pressure monitoring
  - Intravenous (i.v.) glucose and thiamine
  - Emergency measurement of antiepileptic drug levels
  - Emergency measurement of electrolytes and magnesium
  - Full haematological screen
  - Measurement of hepatic and renal function
2. Initial pharmacological treatment of generalised convulsive status epilepticus (GCSE) and non-convulsive status epilepticus (NCSE)
  - Lorazepam followed by phenytoin or fosphenytoin
  - Diazepam followed by phenytoin or fosphenytoin
3. Management of refractory status epilepticus
  - Referral to an intensive care unit
  - Anaesthetic agents such as midazolam, propofol or barbiturates (thiopental, pentobarbital) for GCSE
  - Non-anaesthetic anticonvulsants such as phenobarbital or valproic acid for NCSE

## **MAJOR OUTCOMES CONSIDERED**

- Effectiveness of treatment
- Side effects of pharmacological agents
- Morbidity and mortality

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

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

One member of the Task Force Panel searched available published reports from 1966 to 2005 using the database MEDLINE and EMBASE (last search in January 2005). The search was limited to papers published in English. The subject term 'status epilepticus' was combined with the terms 'controlled clinical trial', 'randomised controlled trial' (RCT), 'multicentre study', 'meta analyses and 'cross over study'. Furthermore, the Cochrane Central Register of Controlled Trials (CENTRAL) was sought. Finally, the websites of the World Health Organisation (WHO), the International League against Epilepsy (ILAE) and the American Neurological Association (ANA) were explored to look for additional information.

### 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 randomised controlled clinical trials with masked outcome assessment in representative populations. The following are required:

- a. Randomisation 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**

Systematic Review

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

The evidence for therapeutic interventions (class I–IV) and the rating of recommendations (level A–C) were classified by using the definitions previously reported (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields).

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

The members of the task force read the first draft of the recommendations and discussed changes (informative consensus approach). Where there was a lack of evidence but consensus was clear the task force members have stated their opinion as good practice points (GPP).

## **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 (GPPs)** Where there was lack of evidence but consensus was clear the Task Force members have stated their opinion as good practice points.

## **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" 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 [GPP]) are defined at the end of the "Major Recommendations" field.

### **General Initial Management**

General management approaches in generalised convulsive, complex partial and subtle status epilepticus (SE) should include: assessment and control of the airways and of ventilation, arterial blood gas monitoring to see if there is metabolic acidosis and hypoxia requiring immediate treatment through airway management and supplemental oxygen, electrocardiogram (ECG) and blood pressure monitoring. Other measures include intravenous (i.v.) glucose and thiamine as required, emergency measurement of antiepileptic drug levels, electrolytes and magnesium, a full haematological screen, and measures of hepatic and renal function. The cause of the status should be identified urgently and may require treatment in its own right (**good practice point [GPP]**).

### **Initial Pharmacological Treatment of Generalised Convulsive SE (GCSE) and Non-convulsive SE (NCSE)**

The initial therapy of NCSE depends on the type and the cause. Subtle SE evolving from GCSE is refractory by nature and its further treatment is described below. Complex partial SE should be treated initially as GCSE. The preferred treatment pathway is i.v. administration of 4 mg of lorazepam; this dose is repeated if seizures continue for more than 10 min after first injection. If necessary, additional phenytoin (15 to 18 mg/kg) or equivalent fosphenytoin is recommended. Alternatively, 10 mg of diazepam directly followed by 15 to 18 mg/kg of phenytoin or equivalent fosphenytoin can be given; if seizures continue for more than 10 min after injection another 10 mg of diazepam is recommended. If necessary, additional lorazepam (4 to 8 mg) should be administered (**Level A rating**).

## **General Management of Refractory Status Epilepticus**

GCSE that does not respond to initial anticonvulsant substances needs to be treated on an intensive care unit (**GPP**).

### **Pharmacological Treatment for Refractory GCSE and Subtle Status Epilepticus**

In GCSE and subtle SE the task force members suggest proceeding immediately to the infusion of anaesthetic doses of midazolam, propofol or barbiturates because of the increasing risk of brain and systemic damage. Due to poor evidence the task force cannot recommend which of the anaesthetic substances should be administered first. They recommend the titration of the anaesthetic against an electroencephalogram (EEG) burst suppression pattern. This goal should be maintained for at least 24 hours. Simultaneously, the chronic antiepileptic medication the patient will be treated with in future should be initiated (**GPP**).

*Barbiturates:* To start with thiopental is administered as a 100 to 200 mg of bolus over 20 sec then further 50 mg of boluses every 2 to 3 min until seizures are controlled, infusion 3 to 5 mg/kg/hour. Pentobarbital (the first metabolite of thiopental) is marketed in the USA as the alternative to thiopental and is given as a bolus dose of 10 to 20 mg/kg followed by an infusion of 0.5 to 1 mg/kg/hour increasing to 1 to 3 mg/kg/hour.

*Midazolam:* Effective initial i.v. doses of midazolam are a 0.2 mg/kg bolus, followed by continuous infusion at rates of 0.1 to 0.4 mg/kg/hour.

*Propofol:* Bolus (i.v.) of 2 mg/kg is administered followed by a continuous infusion of 5 to 10 mg/kg/hour.

In cases of elderly patients in whom intubation and artificial ventilation would not be justified, non-anaesthetising anticonvulsants may be tried (see below) (**GPP**).

### **Pharmacological Treatment for Refractory NCSE**

In complex partial SE, the time that has elapsed until termination of status is less critical compared to GCSE. Thus, general anaesthesia due to its possible severe complications should be postponed and non-anaesthetising anticonvulsants may be tried initially (**GPP**).

*Phenobarbital:* 20 mg/kg i.v., administration of additional boluses requires intensive care conditions.

*Valproic acid:* i.v. bolus of 25 to 45 mg/kg is administered followed by maximum rates up to 6 mg/kg/min.

If the treatment regimen includes the administration of anaesthetics then the same protocol applies as described for refractory GCSE.

### **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 randomised controlled clinical trials with masked outcome assessment in representative populations. The following are required:

- a. Randomisation concealment
- b. Primary outcome(s) is/are clearly defined
- c. Exclusion/inclusion criteria are clearly defined
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**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 Point (GPP)** Where there was lack of evidence but consensus was clear the Task Force members have stated their opinion 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 management of generalised convulsive and non-convulsive status epilepticus

### **POTENTIAL HARMS**

#### **Side Effects of Initial Treatment of Status Epilepticus (SE)**

Safety issues of the common initial anticonvulsants have been compared in patients with generalised convulsive status epilepticus (GCSE) as well as in patients with non-convulsive subtle SE. In GCSE, hypoventilation, hypotension, and cardiac arrhythmias were observed. These side effects were more frequent in subtle SE.

#### **Anaesthetising Anticonvulsants**

- The risks of anaesthesia (e.g., arterial hypotension, gastroparesis, immunosuppression) may be greater than the risks of ongoing non-convulsive epileptic activity.
- Side effects such as arterial hypotension were significantly more frequently seen with pentobarbital compared to midazolam and propofol. Overall mortality was 48% but there was no association between drug selection and the risk of death.

## **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.

## **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**

Getting Better  
Living with Illness

### **IOM DOMAIN**

Effectiveness

## **IDENTIFYING INFORMATION AND AVAILABILITY**

### **BIBLIOGRAPHIC SOURCE(S)**

Meierkord H, Boon P, Engelsen B, Gocke K, Shorvon S, Tinuper P, Holtkamp M. EFNS guideline on the management of status epilepticus. Eur J Neurol 2006 May;13(5):445-50. [40 references] [PubMed](#)

### **ADAPTATION**

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

### **DATE RELEASED**

2006 May

### **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 Task Force on the Management of Status Epilepticus

### **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

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## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Not stated

## **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 Hartmut Meierkord, Department of Neurology, Charité – Universitätsmedizin Berlin, Schumannstrasse 20/21, 10117 Berlin, Germany; Phone: +49 30 450 56 01 05; Fax: +49 30 450 56 09 32; E-mail: [hartmut.meierkord@charite.de](mailto:hartmut.meierkord@charite.de)

## **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 March 26, 2007. The information was verified by the guideline developer on May 3, 2007.

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Date Modified: 11/3/2008

