



Complete Summary

GUIDELINE TITLE

EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias.

BIBLIOGRAPHIC SOURCE(S)

May A, Leone M, Afra J, Linde M, Sandor PS, Evers S, Goadsby PJ, EFNS Task Force. EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. *Eur J Neurol* 2006 Oct;13(10):1066-77. [143 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 information has been released.

- [September 29, 2006 – Lamictal \(lamotrigine\)](#): New preliminary information available regarding the effects of Lamictal on the baby if taken during the first three months of pregnancy.
- [July 19, 2006, Triptans](#): Healthcare professionals and consumers of new safety information regarding taking triptans together with selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs).
- [June 15, 2005, Non-Steroidal Anti-Inflammatory Drugs \(NSAIDs\)](#): U.S. Food and Drug Administration (FDA) recommended proposed labeling for both the prescription and over the counter (OTC) NSAIDs and a medication guide for the entire class of prescription products.
- [April 7, 2005, Non-steroidal anti-inflammatory drugs \(NSAIDs\) \(prescription and OTC, including ibuprofen and naproxen\)](#): FDA asked manufacturers of prescription and non-prescription (OTC) non-steroidal anti-inflammatory drugs (NSAIDs) to revise their labeling to include more specific information about potential gastrointestinal (GI) and cardiovascular (CV) risks.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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SCOPE

DISEASE/CONDITION(S)

- Cluster headache
- Paroxysmal hemicrania
- Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Pharmacology
Preventive Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To give evidence-based recommendations for the treatment of cluster headache, paroxysmal hemicranias, and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome

TARGET POPULATION

Patients suffering from cluster headache, paroxysmal hemicranias, and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

Cluster Headaches

1. 100% oxygen
2. Triptans (e.g., sumatriptan, zolmitriptan)
3. Intranasal lidocaine
4. Subcutaneous octreotide

Prevention

Cluster Headaches

1. Verapamil
2. Steroids
3. Lithium carbonate
4. Methysergide
5. Topiramate
6. Ergotamine tartrate
7. Valproic acid
8. Melatonin
9. Baclofen

Paroxysmal Hemicrania

1. Indomethacin
2. Verapamil
3. Non-steroidal anti-inflammatory drugs (NSAIDs)

Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) Syndrome

1. Lamotrigine
2. Topiramate
3. Gabapentin

MAJOR OUTCOMES CONSIDERED

- Effectiveness of treatment
- Prevention of attacks

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

A literature search was performed using the reference databases MedLine, Science Citation Index and the Cochrane Library; the keywords used were 'cluster headache', 'paroxysmal hemicrania', 'SUNCT', 'treatment' and 'trial' (last search in January 2006). All papers published in English, German or French were considered if they described a controlled trial or a case series on the treatment of at least five patients (or less in paroxysmal hemicrania or short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing [SUNCT] syndrome). Papers discovered by this search were reviewed, as were references cited therein. In addition, review books, the German treatment recommendations for cluster headache were consulted and abstracts with new data from the most recent congress of the International Headache Society (HIS) (Kyoto, October 2005) were hand searched.

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

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The findings in these studies were evaluated according to the recommendations of the European Federation of Neurological Societies (EFNS) resulting in level A, B or C recommendations and good practice points (see the "Availability of Companion Documents" field in this summary).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

All authors performed an independent literature search. All members of the task force read the first draft and discussed changes by email. All recommendations had to be agreed on by all members of the task force unanimously. The background of the research strategy and of reaching consensus and the definitions of the recommendation dosages used in this paper follow the European Federation of Neurological Societies (EFNS) guidelines (see "Availability of Companion Documents" field).

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 point Where there was a lack of evidence but consensus was clear, the Task Force has stated their opinion as good practice points (GPPs).

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).

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.

Table 5. Treatment Recommendations for Cluster Headache, Paroxysmal Hemicrania and Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) Syndrome

Therapy	Treatment of Choice		
	Cluster Headache	Paroxysmal Hemicrania	SUNCT Syndrome
Acute	100% oxygen, 15 l/min (A) Sumatriptan 6 mg, subcutaneous (A) Sumatriptan 20 mg nasal (A) Zolmitriptan 5 mg nasal (A/B) Zolmitriptan 10 mg nasal (A/B) Zolmitriptan 10 mg oral (B) Zolmitriptan 5 mg oral (B) Lidocaine intranasal (B) Octreotide (B)	None	None
Preventative	Verapamil (A) Steroids (A) Lithium carbonate (B) Methysergide (B) Topiramate (B) Ergotamine tartrate (B) Valproic acid (C) Melatonin (C) Baclofen (C)	Indomethacin (A) Verapamil (C) Non-steroidal anti-inflammatory drugs (NSAIDs) (C)	Lamotrigine (C)

For exact doses see original guideline document (**A** denotes effective, **B** denotes probably effective, **C** denotes possibly effective).

Treatment of Cluster Headache

Level A Recommendation

The first option for the treatment of acute attacks of cluster headache should be the inhalation of 100% oxygen with at least 7 l/min over 15 min (**class II trials**) or with the subcutaneous injection of 6 mg sumatriptan (**class I trials**). An alternative would be sumatriptan 20 mg nasal spray or zolmitriptan 5 mg nasal spray (**one class I trial each**), with the disadvantage of a slower onset and the advantage of being able to treat more attacks in 24 hours than with injected sumatriptan.

Prophylaxis of cluster headache should be tried first with verapamil at a daily dose of at least 240 mg (maximum dose depends on efficacy or tolerability, electrocardiogram [ECG] controls are obligatory with increasing doses). Although no class I or II trials are available, steroids are clearly effective for treating cluster headache. Therefore, the use of at least 100 mg methylprednisone (or equivalent corticosteroid) given orally or up to 500 mg intravenously (i.v.) per day over 5 days (then tapering down) is recommended.

Level B Recommendation

Intranasal lidocaine (4%) and subcutaneous octreotide (100 micrograms) can be tried for treating acute cluster headache attacks if level A medication is ineffective or contraindicated. Oral administration of zolmitriptan at 5 to 10 mg is effective in some patients (**class I trial**) but high doses produce more side effects and limit practical use.

Methysergide and lithium are drugs of second choice if verapamil is ineffective or contraindicated. Corticosteroids can be used for short periods where bouts are short or to help establish another medication. Topiramate is promising, but only open trials exist at this point. Melatonin is useful in some patients. Except for lithium, the maximum dose depends on efficacy and tolerability. Ergotamine tartrate is recommended for short-term prophylaxis (**class III studies**). Despite positive class II studies, pizotifen and intranasal capsaicin should only be used in rare cases because of side effects.

Level C Recommendation

Baclofen 15 to 30 mg and valproic acid showed possible efficacy and can be tried as drugs of third choice.

Good Practice Point

Surgical procedures are not indicated in most of the patients with cluster headache. Patients with intractable chronic cluster headache should be referred to centres with expertise in both destructive and neuromodulatory procedures to be offered all reasonable alternatives before a definitive procedure is conducted.

Treatment of Paroxysmal Hemicrania

Paroxysmal hemicrania is to be treated with indomethacin up to 200 mg (**level A recommendation**). Alternatively, verapamil and other NSAIDs can be tried (**level C recommendation**).

Treatment of Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) Syndrome

Recent large case series outcomes suggest that lamotrigine is the treatment of choice in SUNCT, followed by topiramate and gabapentin.

Definitions:

Evidence Classification Scheme for a Therapeutic Intervention

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- a. Randomization concealment
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Rating of Recommendations

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

Good practice point Where there was a lack of evidence but consensus was clear, the Task Force has stated their opinion as good practice points (GPPs).

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 cluster headache, paroxysmal hemicranias, and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome

POTENTIAL HARMS

Adverse Effects of Medications

- The most uncomfortable side effects of sumatriptan are chest pain and distal paresthesia
- Side effects of verapamil are bradycardia, ankle oedema, constipation, gastrointestinal discomfort, gingival hyperplasia and dull headache. Regular echocardiographic (ECG) controls are required to control for an increase in cardiac conduction time reflected in a prolongation of the PR interval. Sometimes, ECG may be necessary because of the negative inotropic effects of verapamil.
- Major side effects of lithium are hyperthyreosis, tremor and renal dysfunction. The plasma level should be monitored and kept between 0.6 and 1.2 mmol/l. Regular control of liver, renal and thyroid function and of electrolytes is required.
- Methysergide should be used with caution when patients are receiving other ergotamine derivatives or triptans. As there is a definite incidence of pulmonary and retroperitoneal fibrosis under long-term use, the continuous use of methysergide is limited to 6 months.
- Main side effects of topiramate are cognitive disturbances, paresthesias, and weight loss.
- A proton pump inhibitor should be given with indomethacin as gastrointestinal discomfort and bleeding are the major side effects of indomethacin.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Contraindications to sumatriptan are cardio- and cerebrovascular disorders and untreated arterial hypertension.
- Topiramate is contraindicated in nephrolithiasis.

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)

May A, Leone M, Afra J, Linde M, Sandor PS, Evers S, Goadsby PJ, EFNS Task Force. EFNS guidelines on the treatment of cluster headache and other trigeminal-

autonomic cephalalgias. Eur J Neurol 2006 Oct;13(10):1066-77. [143 references]
[PubMed](#)

ADAPTATION

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

DATE RELEASED

2006 Oct

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 Treatment of Cluster Headache and other Trigeminal Autonomic Cephalalgias

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: A. May, Department of Systems Neuroscience, University of Hamburg, Hamburg, Germany; M. Leone, Istituto Neurologico Carlo Besta, Milan, Italy; J. Áfra, National Institute of Neurosurgery, Budapest, Hungary; M. Linde, Cephalaea Pain Centre and Institute of Neuroscience and Physiology, Sahlgren Academy, Göteborg University, Göteborg, Sweden; P. S. Sándor, Department of Neurology, University of Zurich, Zurich, Switzerland; S. Evers, Department of Neurology, University of Münster, Münster, Germany; P. J. Goadsby, Institute of Neurology, Queen Square, London, UK

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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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 Arne May MD, Department of Systems Neuroscience, Universitäts-Krankenhaus Eppendorf (UKE), Martinistr. 52, D-20246 Hamburg, Germany; Phone: 040 42803 9189; Fax: 040 42803 9955; E-mail: a.may@uke.uni-hamburg.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

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