

## \*\*\* Drug Safety Alert \*\*\*

May 6, 2013, the U.S. Food and Drug Administration (FDA) advised health care professionals and women that the anti-seizure medication valproate sodium and related products, valproic acid and divalproex sodium, are contraindicated and should not be taken by pregnant women for the prevention of migraine headaches. Based on information from a recent study, there is evidence that these medications can cause decreased IQ scores in children whose mothers took them while pregnant. Stronger warnings about use during pregnancy will be added to the drug labels, and valproate's pregnancy category for migraine use will be changed from "D" (the potential benefit of the drug in pregnant women may be acceptable despite its potential risks) to "X" (the risk of use in pregnant women clearly outweighs any possible benefit of the drug).

Valproate products will remain in pregnancy category D for treating epilepsy and manic episodes associated with bipolar disorder.

**BACKGROUND:** Valproate products are approved for the treatment of certain types of epilepsy, the treatment of manic episodes associated with bipolar disorder, and the prevention of migraine headaches. They are also used off-label (for uses not approved by FDA) for other conditions, particularly other psychiatric conditions.

This alert is based on the final results of the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study showing that children exposed to valproate products while their mothers were pregnant had decreased IQs at age 6 compared to children exposed to other anti-epileptic drugs. For additional details, see the Drug Safety Communication Data Summary section.

**RECOMMENDATION:** Valproate products should not be used in pregnant women for prevention of migraine headaches and should be used in pregnant women with epilepsy or bipolar disorder only if other treatments have failed to provide adequate symptom control or are otherwise unacceptable.

Women who are pregnant and taking a valproate medication should not stop their medication but should talk to their health care professionals immediately. Stopping valproate treatment suddenly can cause serious and life-threatening medical problems to the woman or her baby.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

Complete and submit the report Online: [www.fda.gov/MedWatch/report.htm](http://www.fda.gov/MedWatch/report.htm)

Download form or call [1-800-332-1088](tel:1-800-332-1088) to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

Read the complete MedWatch safety alert, including a link to the Drug Safety Communication at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm350868.htm>.

## Health Care Guideline

# Diagnosis and Treatment of Headache

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### How to Cite this Document

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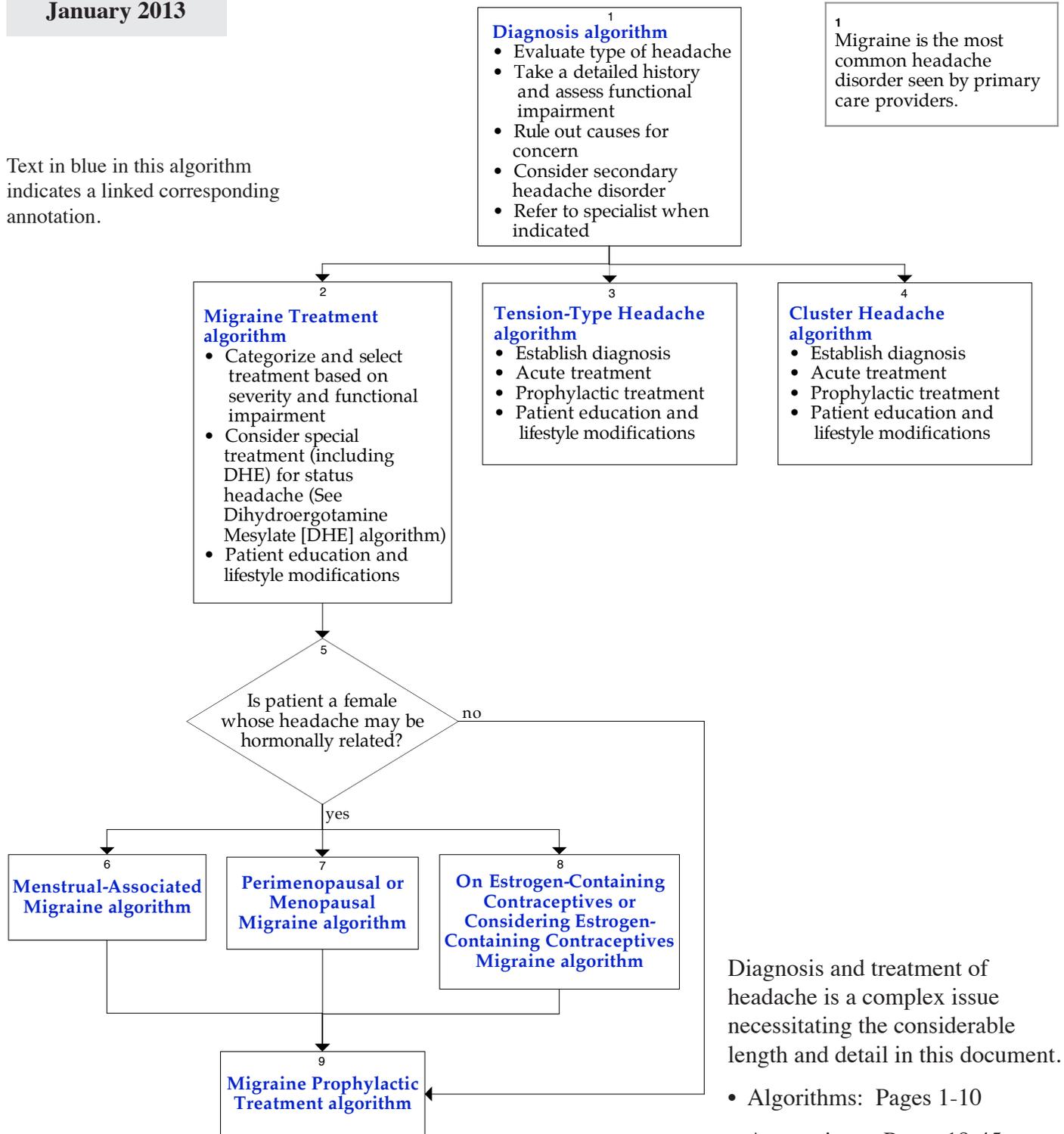
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**Eleventh Edition  
January 2013**

**Main Algorithm**

Text in blue in this algorithm indicates a linked corresponding annotation.

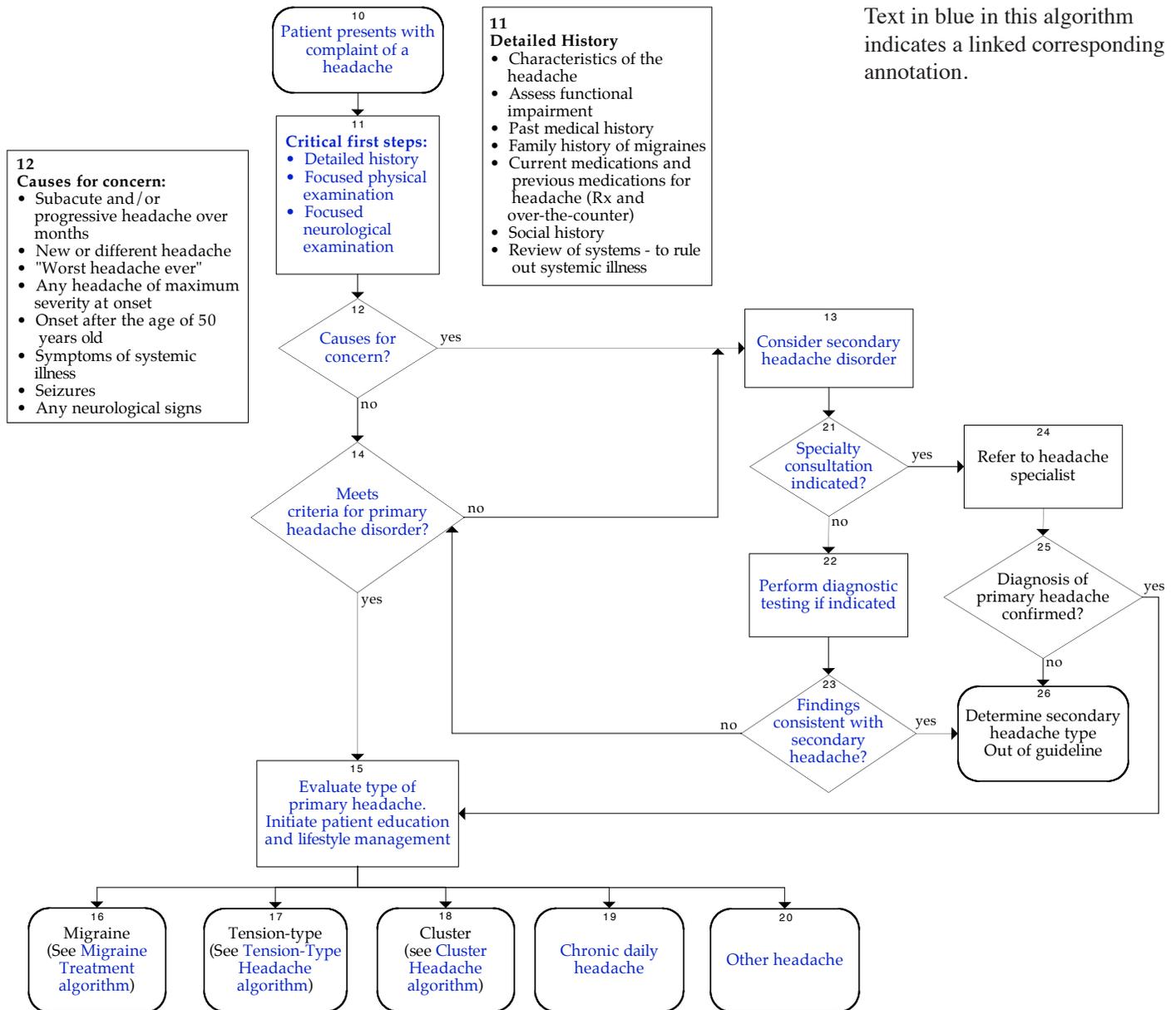


Diagnosis and treatment of headache is a complex issue necessitating the considerable length and detail in this document.

- Algorithms: Pages 1-10
- Annotations: Pages 18-45
- Drug Tables: Pages 76-80

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## Diagnosis Algorithm



### Sinus Headache

15

Migraine-associated symptoms are often misdiagnosed as "sinus headache" by patients and clinicians. Most headaches characterized as "sinus headaches" are migraines.

The International Classifications of Headache Disorders (ICHD-II) defines sinus headache by purulent nasal discharge, pathologic sinus finding by imaging, simultaneous onset of headache and sinusitis, and headache localized to specific facial and cranial areas of the sinuses.

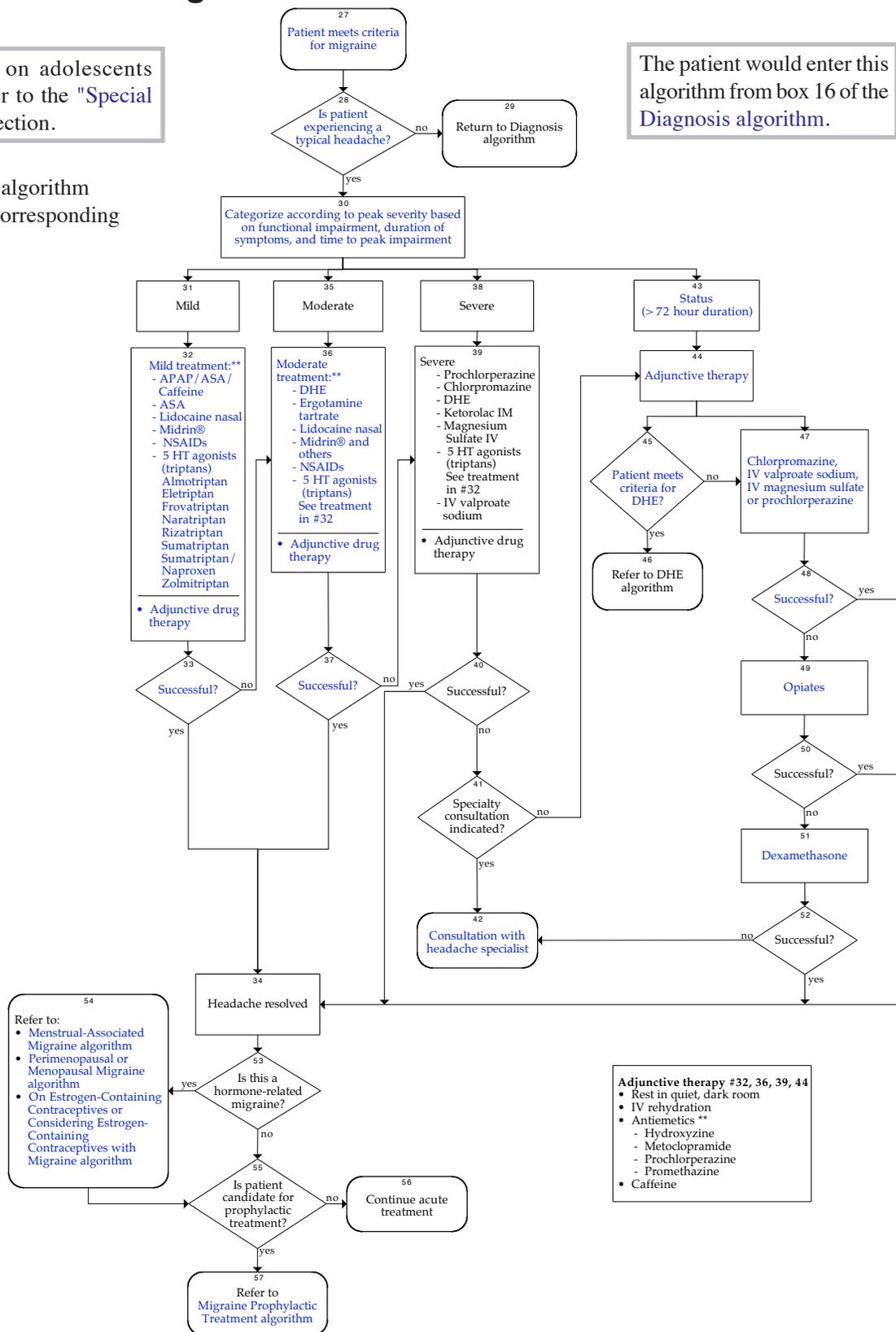
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# Migraine Treatment Algorithm

For information on adolescents (ages 12-17), refer to the "Special Circumstances" section.

The patient would enter this algorithm from box 16 of the Diagnosis algorithm.

Text in blue in this algorithm indicates a linked corresponding annotation.



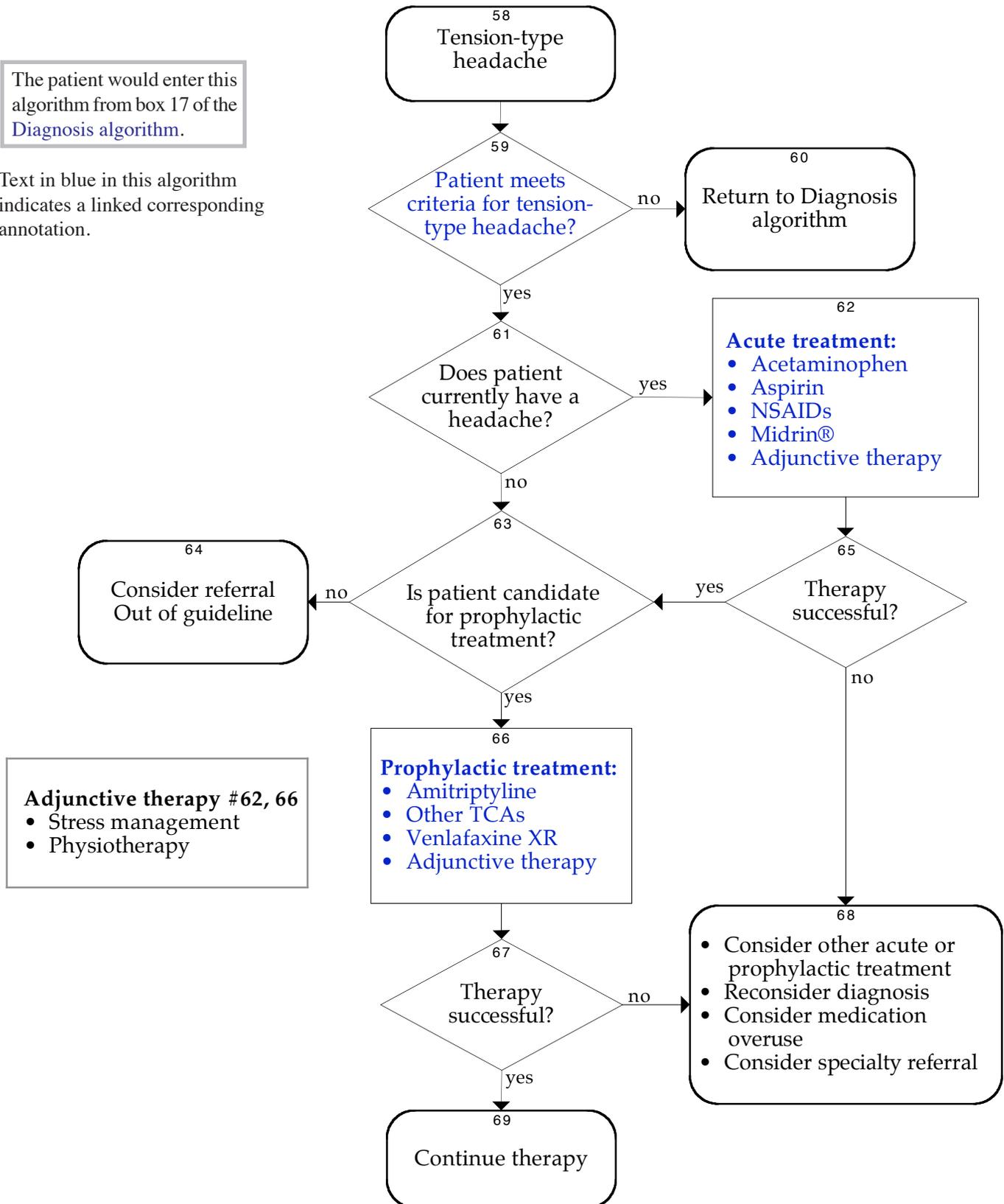
**Adjunctive therapy #32, 36, 39, 44**

- Rest in quiet, dark room
- IV rehydration
- Antiemetics \*\*
  - Hydroxyzine
  - Metoclopramide
  - Prochlorperazine
  - Promethazine
- Caffeine

## Tension-Type Headache Algorithm

The patient would enter this algorithm from box 17 of the Diagnosis algorithm.

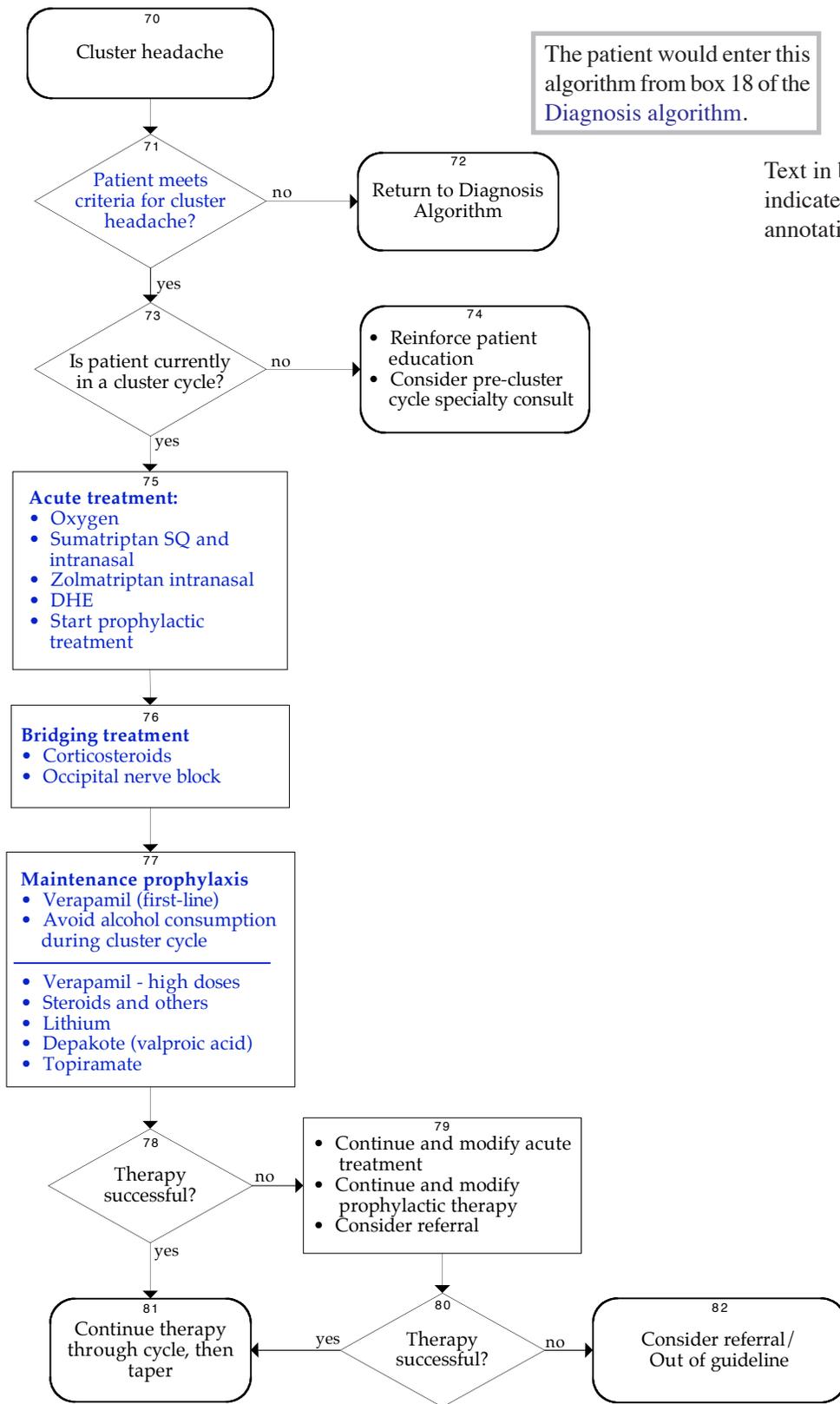
Text in blue in this algorithm indicates a linked corresponding annotation.



**Adjunctive therapy #62, 66**

- Stress management
- Physiotherapy

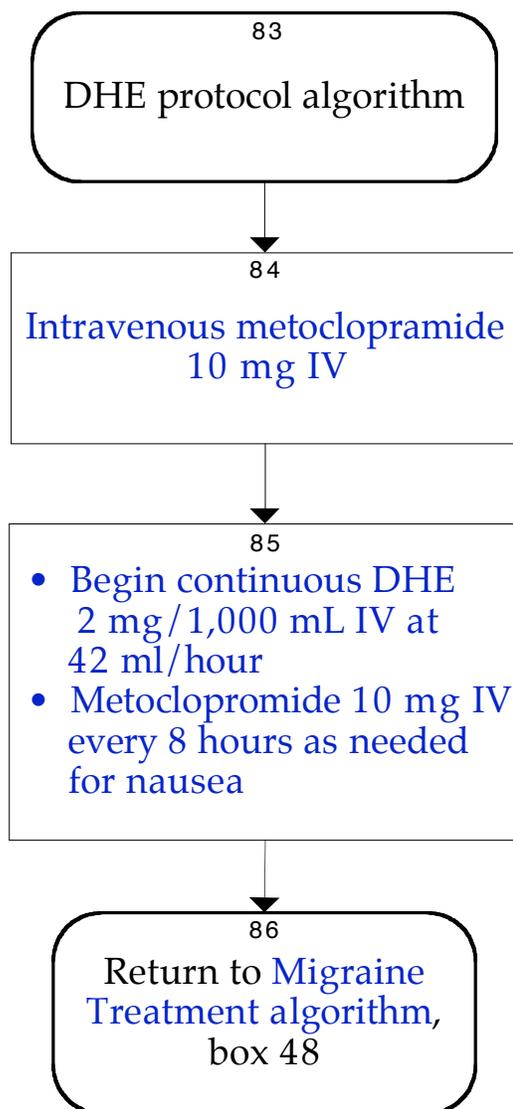
## Cluster Headache Algorithm



The patient would enter this algorithm from box 18 of the Diagnosis algorithm.

Text in blue in this algorithm indicates a linked corresponding annotation.

## Dihydroergotamine Mesylate (DHE) Algorithm



The patient would enter this algorithm from box 46 of the [Migraine Treatment algorithm](#).

Text in blue in this algorithm indicates a linked corresponding annotation.

**Caution:** Dihydroergotamine mesylate must not be given to or continued in patients who develop the following conditions:

- Pregnancy
- History of ischemic heart disease
- History of Prinzmetal's angina
- Severe peripheral vascular disease
- Onset of chest pain following administration of test dose
- Within 24 hours of receiving any triptan or ergot derivative
- Elevated blood pressure
- Patients with hemiplegic or basilar-type migraines\*
- Cerebrovascular disease

\* Basilar-type migraine is defined as three of the following features: diplopia, dysarthria, tinnitus, vertigo, transient hearing loss or mental confusion (*Headache Classification Subcommittee of the International Headache Society, 2004 [Guideline]*).

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## Menstrual-Associated Migraine Algorithm

The patient would enter this algorithm from box 54 of the Migraine Treatment algorithm.

Text in blue in this algorithm indicates a linked corresponding annotation.

Menstrual only

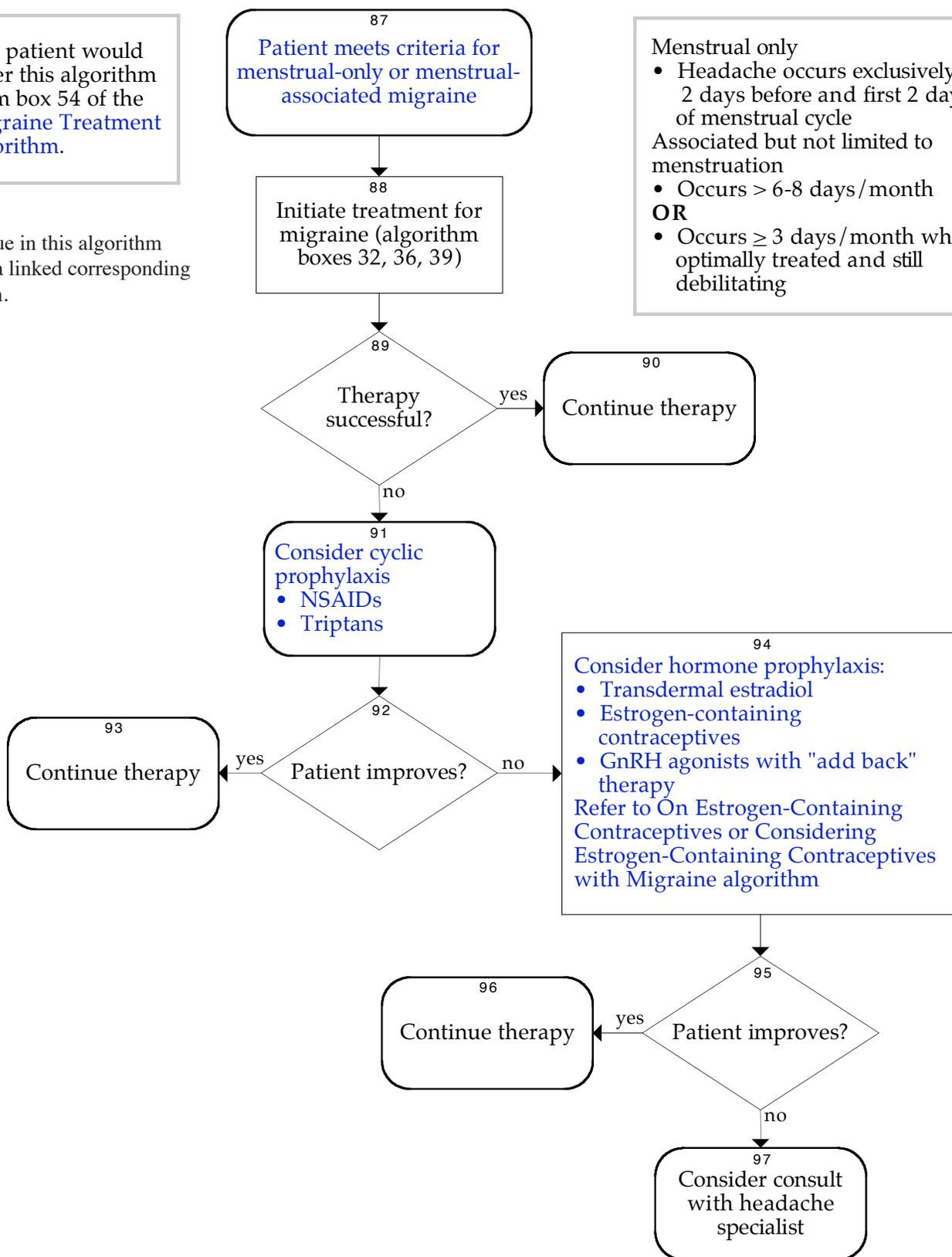
- Headache occurs exclusively 2 days before and first 2 days of menstrual cycle

Associated but not limited to menstruation

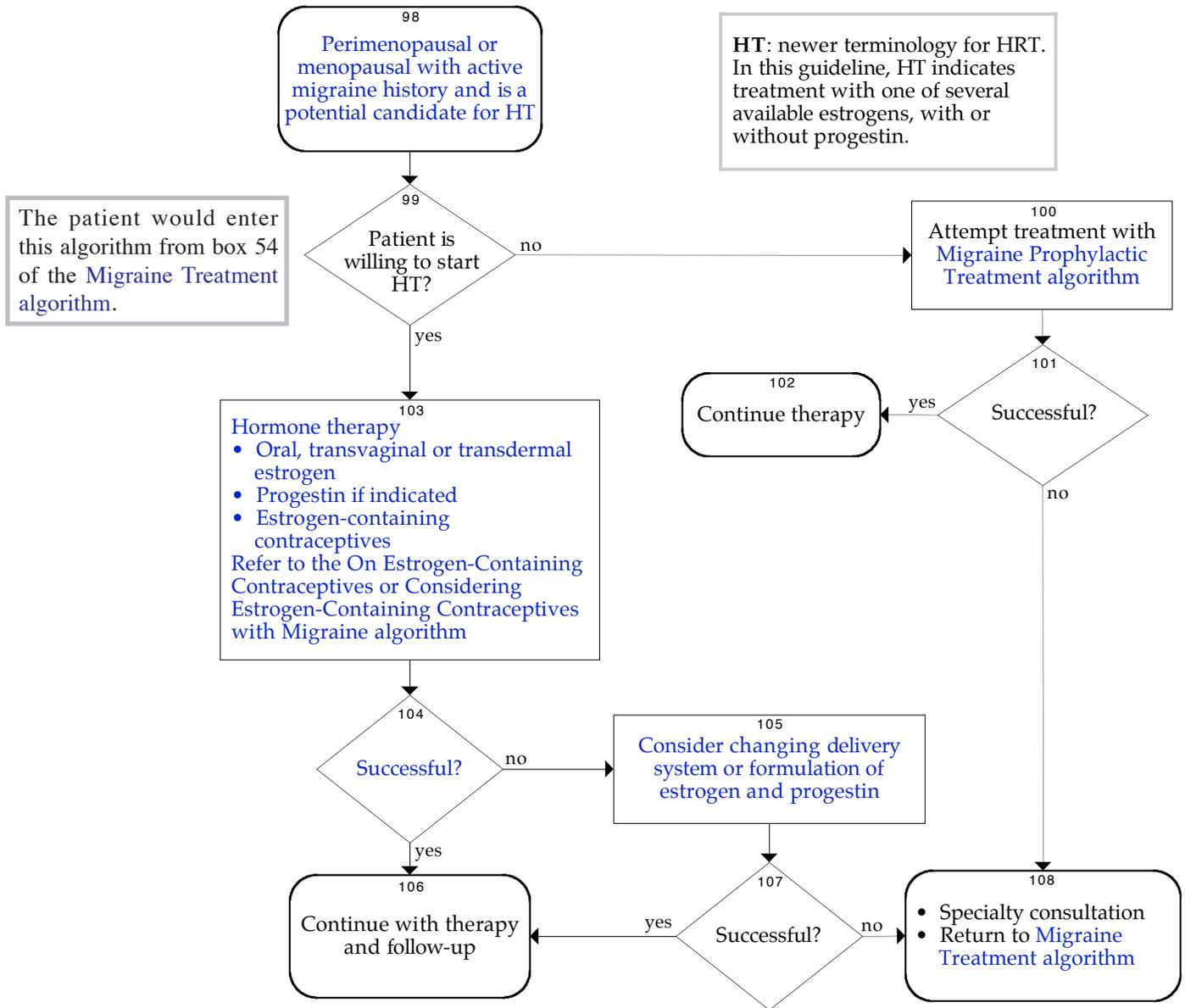
- Occurs > 6-8 days/month

**OR**

- Occurs  $\geq$  3 days/month when optimally treated and still debilitating



## Perimenopausal or Menopausal Migraine Algorithm



HT: newer terminology for HRT. In this guideline, HT indicates treatment with one of several available estrogens, with or without progestin.

The patient would enter this algorithm from box 54 of the Migraine Treatment algorithm.

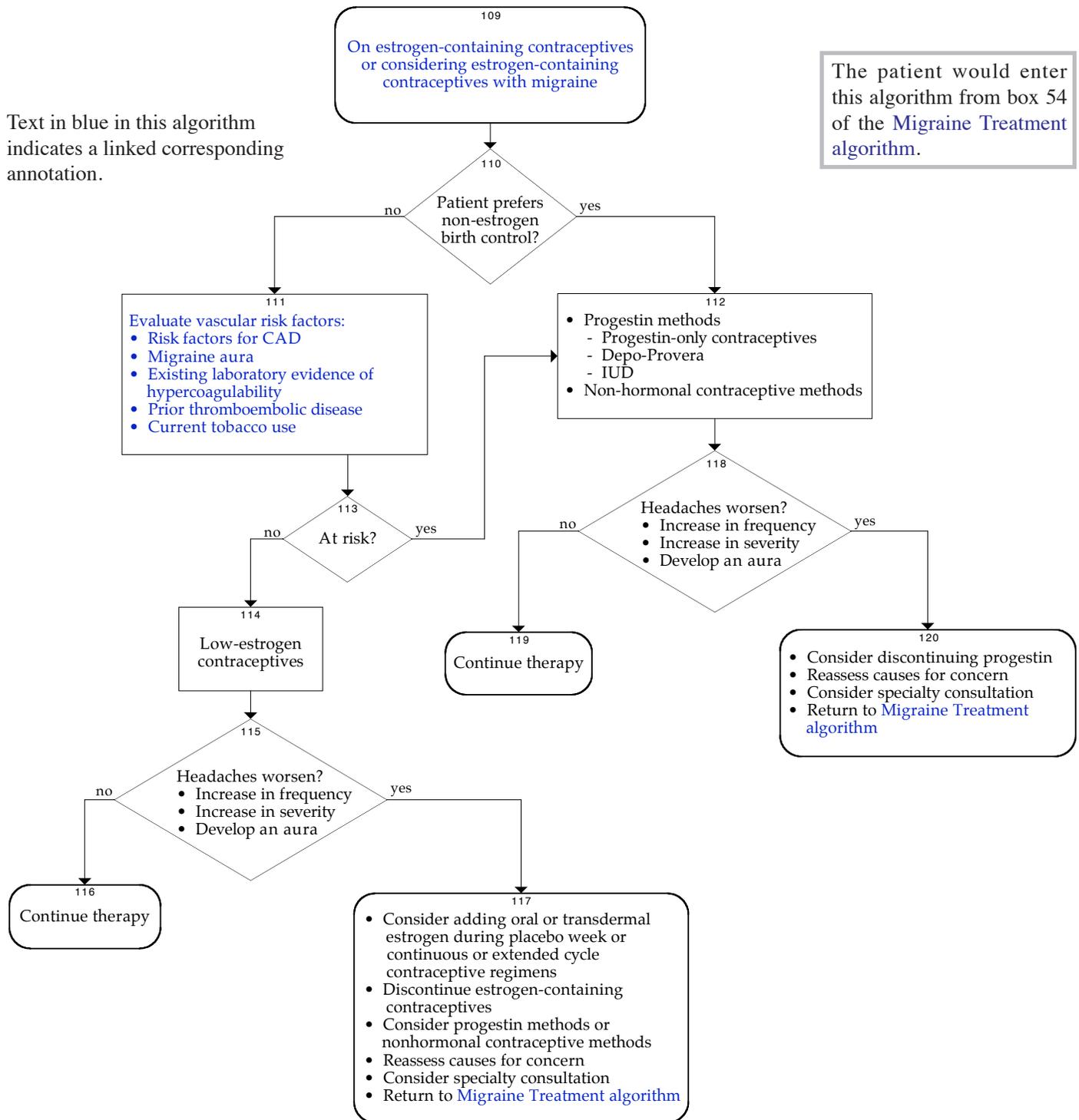
Text in blue in this algorithm indicates a linked corresponding annotation.

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## On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine Algorithm

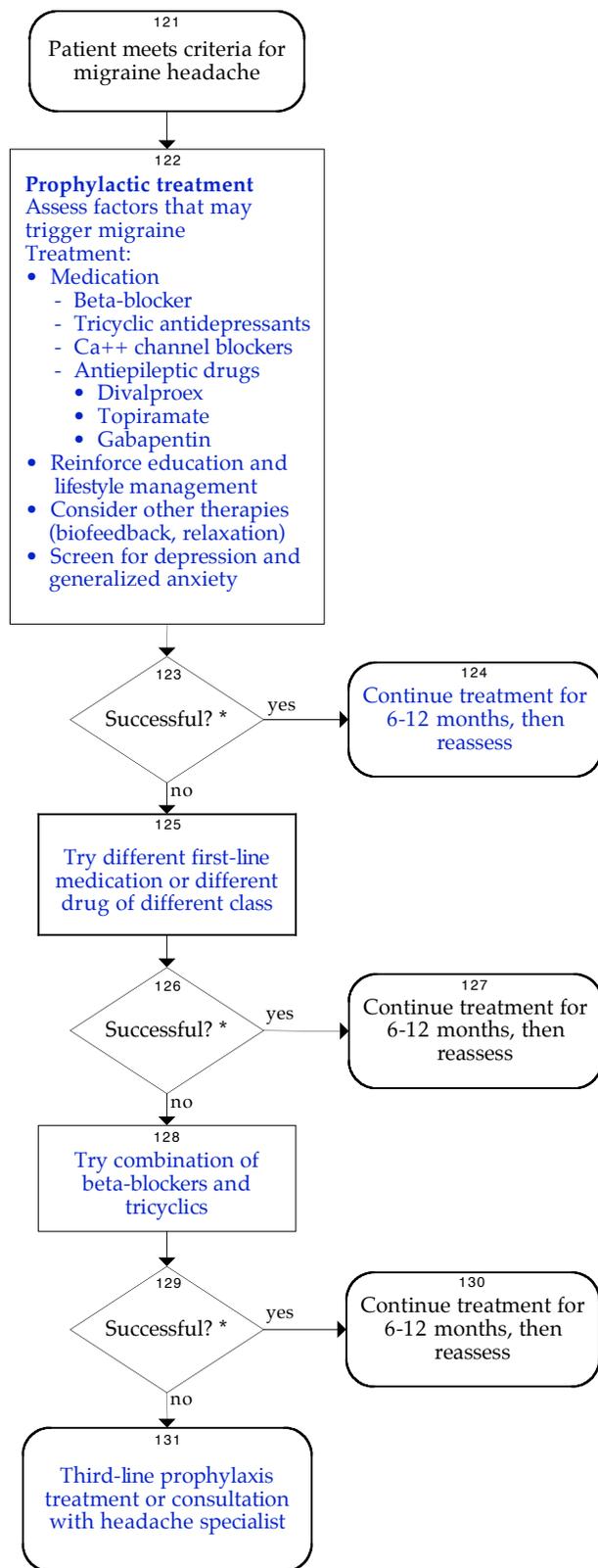
Text in blue in this algorithm indicates a linked corresponding annotation.

The patient would enter this algorithm from box 54 of the [Migraine Treatment algorithm](#).



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## Migraine Prophylactic Treatment Algorithm



Text in blue in this algorithm indicates a linked corresponding annotation.

Patients enter this algorithm from box 57 of the Migraine Treatment algorithm.

\*123, 126, 129. Successful? Success as determined by:

- Headaches decrease by 50% or more
- An acceptable side effect profile

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## **Evidence Grading**

### **Literature Search**

A consistent and defined process is used for literature search and review for the development and revision of ICSI guidelines. The literature search was divided into two stages to identify systematic reviews, (stage I) and randomized controlled trials, meta-analysis and other literature (stage II). Literature search terms used for this revision are below and include diagnosis of headache, migraine treatment, tension-type headache treatment, cluster headache treatment, menstrual-associated migraine treatment, perimenopause or menopause migraine treatment, pharmacologic treatment of headache, Botox and headache from June 2010 through July 2012

### **GRADE Methodology**

Following a review of several evidence rating and recommendation writing systems, ICSI has made a decision to transition to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.

GRADE has advantages over other systems including the current system used by ICSI. Advantages include:

- developed by a widely representative group of international guideline developers;
- explicit and comprehensive criteria for downgrading and upgrading quality of evidence ratings;
- clear separation between quality of evidence and strength of recommendations that includes a transparent process of moving from evidence evaluation to recommendations;
- clear, pragmatic interpretations of strong versus weak recommendations for clinicians, patients and policy-makers;
- explicit acknowledgement of values and preferences; and
- explicit evaluation of the importance of outcomes of alternative management strategies.

### **This document is in transition to the GRADE methodology**

Transition steps incorporating GRADE methodology for this document include the following:

- Priority placed upon available Systematic Reviews in literature searches.
- All existing Class A (RCTs) studies have been considered as high quality evidence unless specified differently by a work group member.
- All existing Class B, C and D studies have been considered as low quality evidence unless specified differently by a work group member.
- All existing Class M and R studies are identified by study design versus assigning a quality of evidence. Refer to Crosswalk between ICSI Evidence Grading System and GRADE.
- All new literature considered by the work group for this revision has been assessed using GRADE methodology.

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**Evidence Grading**

**Crosswalk between ICSI Evidence Grading System and GRADE**

<b>ICSI GRADE System</b>	<b>Previous ICSI System</b>
<b>High</b> , if no limitation	<b>Class A:</b> Randomized, controlled trial
<b>Low</b>	<b>Class B:</b> [observational] Cohort study
<b>Low</b> <b>Low</b> <b>*Low</b>	<b>Class C:</b> [observational] Non-randomized trial with concurrent or historical controls Case-control study Population-based descriptive study Study of sensitivity and specificity of a diagnostic test
* Following individual study review, may be elevated to Moderate or High depending upon study design	
<b>Low</b>	<b>Class D:</b> [observational] Cross-sectional study Case series Case report
<b>Meta-analysis</b> <b>Systematic Review</b> <b>Decision Analysis</b> <b>Cost-Effectiveness Analysis</b>	<b>Class M:</b> Meta-analysis Systematic review Decision analysis Cost-effectiveness analysis
<b>Low</b> <b>Low</b> <b>Low</b>	<b>Class R:</b> Consensus statement Consensus report Narrative review
<b>Guideline</b>	<b>Class R:</b> Guideline
<b>Low</b>	<b>Class X:</b> Medical opinion

**Evidence Definitions:**

**High Quality Evidence** = Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate Quality Evidence** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low Quality Evidence** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate or any estimate of effect is very uncertain.

In addition to evidence that is graded and used to formulate recommendations, additional pieces of literature will be used to inform the reader of other topics of interest. This literature is not given an evidence grade and is instead identified as a **Reference** throughout the document.

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# Foreword

## Introduction

This guideline discusses the headache disorders most commonly seen in primary care offices. It is not a comprehensive discussion of diagnosis and treatment of all headache syndromes, since many headaches are rare and felt best treated by headache specialists or neurologists with specialization in headache. It is intended for primary care clinicians to help with their diagnosis and treatment of four main types of headache: migraine, tension-type headache, cluster headache and chronic daily headache. This guideline is necessarily long and may be considered by some to be cumbersome. However, extensive information pertaining to headaches is covered, along with the typical medications. As there are multiple easy-to-access information sources available containing current detailed drug information, drug tables in the appendices highlight only selected drugs whose dosing, side effects and contraindications might otherwise be challenging to locate.

For most headaches, diagnosis is made on the basis of history and physical exam with no imaging or laboratory assistance. There are, however, causes for concern listed in the algorithms, which may direct clinicians to specific testing or referral.

Headache is a very common problem presenting to primary care clinicians, with about 3% of emergency department visits and 1.3% of outpatient visits for headaches. While tension-type headache is the most common type of headache overall, migraine is the most common headache type seen in clinical practice, with visits for tension-type headache and cluster headaches being much less common in clinician's offices. Therefore migraine is the first and primary headache type reviewed.

Migraine is a genetically influenced chronic brain condition marked by paroxysmal attacks of moderate to severe throbbing headache. About 324 million persons suffer from migraine worldwide according to the World Health Organization. Nearly 18% of women and 8% of men in the United States suffer from migraine in any given year. Typically the disorder begins in adolescence and young adults but the lifetime cumulative incidence is 43% for women and 18% for men. Over 25% of migraine sufferers have more than three headache days per month (*Loder, 2010 [Low Quality Evidence]*).

Women headache sufferers may present with a hormonal component to the course of headaches over their lifetime, and an algorithm for treatment of hormone-related headache is also included. Headaches over three times a month are often treated with prophylactic treatment as overuse of medication for acute migraine may actually cause chronic headache.

Because headache is such a common disorder that is often misdiagnosed and undertreated or mistreated, improved diagnosis of headache syndromes will improve the patient's experience of care, notably quality of and satisfaction with care. Morbidity due to headaches is substantial, so improved diagnosis and treatment will improve the health of the population. Reducing office visits, emergency department visits, and inpatient admissions for uncontrolled headache syndromes along with reducing unnecessary tests and procedures for headache diagnosis is likely to reduce total costs of care even if there are more visits for diagnosis of headache and increased costs for headache-specific drugs.

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## Scope and Target Population

Patients age 12 years and older who present with headache. For the purpose of this guideline, pain that primarily involves the back of the neck and only involves the head to a limited extent is not considered a headache. This guideline does not specifically address occipital neuralgia.

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## Aims

1. Increase the accurate diagnosis of primary headaches in patients age 12 years and older. (*Annotation #11*)
2. Increase the percentage of patients with primary headache diagnosis who receive educational materials about headache. (*Annotation #15*)
3. Increase the percentage of patients with primary headache syndrome who receive prophylactic treatment. (*Annotations #66, 77, 91, 94, 122, 131*)
4. Increase the percentage of patients with migraine headache who have improvement in their functional status. (*Annotation #15*)
5. Increase the percentage of patients with migraine headache who have a treatment plan or report adherence to a treatment plan. (*Annotations #32, 33, 36, 42, 43, 44*)
6. Decrease the percentage of patients with migraine headache who are prescribed opiates and barbiturates for the treatment of migraines to less than 5%. (*Annotations #36, 49*)
7. Increase the percentage of patients with migraine headache who have appropriate acute treatment. (*Annotations #30, 32, 36*)

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## Clinical Highlights

- Headache is diagnosed by history and physical examination with limited need for imaging or laboratory tests. (*Annotation #11; Aim #1*)
- Warning signs of possible disorder other than primary headache are (*Annotation #12; Aim #1*):
  - Subacute and/or progressive headaches that worsen over time (months)
  - A new or different headache
  - Any headache of maximum severity at onset
  - Headache of new onset after age 50
  - Persistent headache precipitated by a Valsalva maneuver
  - Evidence such as fever, hypertension, myalgias, weight loss or scalp tenderness suggesting a systemic disorder
  - Presence of neurological signs that may suggest a secondary cause
  - Seizures
- Migraine-associated symptoms are often misdiagnosed as "sinus headache" by patients and clinicians. Most headaches characterized as "sinus headaches" are migraines. (*Annotation #15; Aim #1*).
- Early treatment of migraines with effective medications improves a variety of outcomes including duration, severity and associated disability. (*Annotations #32, 36; Aim #7*)

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- Drug treatment of acute headache should generally not exceed more than two days per week on a regular basis. More frequent treatment other than this may result in medication-overuse chronic daily headaches. (*Annotations #32, 36; Aim #7*)
- Inability to work or carry out usual activities during a headache is an important issue for migraineurs. (*Annotation #30; Aim #4*)
- Prophylactic therapy should be considered for all patients. (*Annotations #66, 77, 91, 94, 122, 131; Aim #3*)
- Migraines occurring in association with menses and not responsive to standard cyclic prophylaxis may respond to hormonal prophylaxis with the use of estradiol patches, creams or estrogen-containing contraceptives. (*Annotation #94; Aim #3*)
- Women who have migraines with aura have a substantially higher risk of stroke with the use of estrogen-containing contraceptive compared to those without migraines. Headaches occurring during perimenopause or after menopause may respond to hormonal therapy. (*Annotations #109, 111; Aim #5*)
- Most prophylactic medications should be started in a low dose and titrated to a therapeutic dose to minimize side effects and maintained at target dose for 8-12 weeks to obtain maximum efficacy. (*Annotation #122; Aims #3, 5, 7*)

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## **Implementation Recommendation Highlights**

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

- Develop a system for assessment of headache based on history and functional impairment.
- Develop a system for results of this assessment to be used for identification of treatment options/recommendations.
- Develop systems that allow for consistent documentation and monitoring based on type of headache.
- Develop a system for follow-up assessment that identifies success in management of headache in the primary care setting.
- Develop a process that will remove barriers to referral to a specialist if indicated.
- Develop a system for consistent documentation and monitoring of medication administration.

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## **Related ICSI Scientific Documents**

### **Guidelines**

- [Assessment and Management of Chronic Pain](#)

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## **Definition**

**Clinician** – All health care professionals whose practice is based on interaction with and/or treatment of a patient.

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## Special Circumstances

### Adolescents

At this time the majority of the adolescent literature supports a strong placebo effect in this age group. Success of triptans and prophylactic medications in patients age 12-17 yield similar positive outcomes as in adult studies, but placebo administered in blinded, controlled studies has a similar effect. There has been a recent study that supports the use of almotriptan with statistically significant efficacy over placebo. As an acute treatment, almotriptan in the dose of 12.5 mg was effective in relieving pain and associated symptoms and was well tolerated (*Linder, 2008 [High Quality Evidence]*).

As a prophylactic treatment, topiramate 100 mg/day was effective in reduction of the number of migraine headaches a month (*Lewis, 2009 [High Quality Evidence]*).

Psychological treatments, principally relaxation and cognitive behavioral therapies are effective treatments of childhood headache (*Eccleston, 2009 [Meta-analysis/Systematic Review]*).

### Pregnancy and Breastfeeding

Special consideration should be given to medication selection and management during pregnancy and breastfeeding, considering the risks and benefits of selected drugs and their efficacy.

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# Algorithm Annotations

## Diagnosis Algorithm Annotations

### 10. Patient Presents with Complaint of a Headache

#### Recommendation:

- Clinicians should perform an appropriate prompt evaluation of the patient who presents with headache and initiate acute treatment.

Migraine is the most common headache disorder seen by primary care clinicians (*Tepper, 2004 [Low Quality Evidence]*).

A patient may present for care of headaches during an attack or during a headache-free period. If a patient presents during a headache, appropriate evaluation (history, examination, appropriate testing) needs to be in a timely fashion. Once the diagnosis of primary headache is established, acute treatment is instituted. If the patient has a history of recurrent headaches, a plan for treatment (acute and prophylactic) needs to be established.

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### 11. Critical First Steps

#### Recommendation:

- Clinicians should gather a detailed history, including a focused physical and neurological exam, of the patient who presents with headache.

Headache is one of the most frequent diseases seen in clinics by health care clinicians.

Clinicians, minimal general physical examination is performed at the first consultation of patient presenting with a headache.

Symptoms and signs with the use of criteria can diagnose headache. The International Classification of Headache Disorders, second edition (ICHD-II) system presently provides the gold standard. As empirical evidence and clinical experience accumulate, criteria for diagnosing headaches will be revised (*Olsen, 2006 [Reference]*).

#### Detailed History

Inquire about functional disabilities at work, school, housework or leisure activities during the past three months (informally or using well-validated disability questionnaire).

Assessment of the headache characteristics requires determination of the following:

Temporal profile:

- Time from onset to peak
- Usual time of onset (season, month, menstrual cycle, week, hour of day)
- Frequency and duration
- Stable or changing over past six months and lifetime

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**Algorithm Annotations**

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Autonomic features:

- Nasal stuffiness
- Rhinorrhea
- Tearing
- Eyelid ptosis or edema

Descriptive characteristics: pulsatile, throbbing, pressing, sharp, etc.

Location: uni- or bilateral, changing sides

Severity

Precipitating features and factors that aggravate and/or relieve the headache

Factors that relieve the headache

History of other medical problems

Pharmacological and non-pharmacological treatments that are effective or ineffective

Aura (present in approximately 15% of migraine patients)

**Focused physical examination**

Vital signs (blood pressure, pulse, respirations and temperature)

Extracranial structure evaluation such as carotid arteries, sinuses, scalp arteries, cervical paraspinal muscles

Examination of the neck in flexion versus lateral rotation for meningeal irritation. (Even a subtle limitation of neck flexion may be considered an abnormality.)

**Focused neurological examination**

A focused neurological examination may be capable of detecting most of the abnormal signs likely to occur in patients with headache due to acquired disease or a secondary headache.

This examination should include at least the following evaluations:

- Assessment of patient's awareness and consciousness, presence of confusion, and memory impairment
- Ophthalmological examination to include pupillary symmetry and reactivity, optic fundi, visual fields, and ocular motility
- Cranial nerve examination to include corneal reflexes, facial sensation and facial symmetry
- Symmetry of muscle tone, strength (may be as subtle as arm or leg drift), or deep tendon reflexes
- Sensation
- Plantar response(s)
- Gait, arm and leg coordination

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## **12. Causes for Concern?**

Headache features beyond that of International Classification of Headache Disorders, second edition (ICHD-II) system criteria should raise concern of a more sinister underlying cause (*Pryse-Phillips, 1997 [Guideline]*).

Causes for concern in the diagnosis of headaches may alter a diagnosis of migraine to a secondary diagnosis of headache, which can be more serious and/or life-threatening (*Dalessio, 1994 [Guideline]; Edmeads, 1988 [Low Quality Evidence]*).

Causes for concern must be evaluated irrespective of the patient's past history of headache. Warning signs of possible disorder other than primary headache are:

- Subacute and/or progressive headaches that worsen over time (months).
- A new or different headache or a statement by a headache patient that "this is the worst headache ever."
- Any headache of maximum severity at onset.
- Headaches of new onset after the age of 50 years old.
- Persistent headache precipitated by a Valsalva maneuver such as cough, sneeze, bending or with exertion (physical or sexual).
- Evidence such as fever, hypertension, myalgias, weight loss or scalp tenderness suggesting a systemic disorder.
- Neurological signs that may suggest a secondary cause. For example: meningismus, confusion, altered levels of consciousness, changes or impairment of memory, papilledema, visual field defect, cranial nerve asymmetry, extremity drifts or weaknesses, clear sensory deficits, reflex asymmetry, extensor plantar response, or gait disturbances.
- Seizures.

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## **13. Consider Secondary Headache Disorder**

The presence of the symptoms or signs listed above suggests a secondary cause for the headache and could be indicative of an underlying organic condition. Alternate diagnoses include subarachnoid hemorrhage, tumor, meningitis, encephalitis, temporal arteritis, idiopathic intracranial hypertension and cerebral venous thrombosis, among others.

### **Secondary Headaches**

- **Subacute and/or progressive, worsening headaches over weeks to months:**

Headaches that worsen with time may be due to a progressive intracranial lesion such as tumor, subdural hematoma, or hydrocephalus. While the neurologic examination may reveal abnormalities that suggest a sinister process, this is not always the case. Accordingly, a history of a progressive headache is an indication for head imaging. For most processes, magnetic resonance imaging with and without gadolinium contrast will be more sensitive than a computed tomography head scan. Note: in patients who receive gadolinium contrast media used in MRI, there is the potential for renal toxicity and the rare complication (3-5% risk in patients with moderate to end-stage renal disease) of life-threatening nephrogenic systemic fibrosis. It is recommended that gadolinium use be avoided when possible in patients with advanced renal disease.

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- **A new or different headache or a statement by a headache patient that "this is the worst headache of my life":**

Primary headache disorders (mainly tension-type headache and migraine) are exceedingly common. A history of a primary headache disorder does not confer protection against a new, serious process that presents with headache. The acuteness of a headache will largely define the differential diagnosis. Headache that presents suddenly, "like a thunderclap," can be characteristic of several serious intracranial processes, including subarachnoid hemorrhage, venous sinus thrombosis, bacterial meningitis, spontaneous cerebral spinal fluid leak, carotid dissection, and rarely, pituitary apoplexy and hypertensive encephalopathy. The first investigation is a computed tomography head scan without contrast. If there is no evidence of a subarachnoid hemorrhage, a lumbar puncture should be performed. If both studies are normal and the suspicion of subarachnoid hemorrhage is still high, a magnetic resonance imaging with and without gadolinium should be obtained. Neurological consultation is indicated and further tests for consideration include magnetic resonance angiogram and magnetic resonance venogram.

If the headache is more subacute in onset, chronic meningitis may need to be considered along with a space-occupying intracranial lesion or hydrocephalus. Again, neuroimaging should be performed. Whether a lumbar puncture is done will be guided by the index of suspicion regarding a meningeal process (e.g., meningitis).

- **Headache of sudden onset:**

This refers mainly to thunderclap headache (see above). It should be treated as an emergency since the possible presence of aneurysmal subarachnoid hemorrhage needs to be assessed as outlined above. Other secondary causes of headache will be found less commonly.

- **Headache precipitated by a Valsalva maneuver such as cough, sneeze, bending or with exertion:**

Valsalva headaches, while often representing primary cough headache, can signal an intracranial abnormality, usually of the posterior fossa. The most commonly found lesion is a Chiari malformation, although other posterior fossa lesions are sometimes found. Less commonly there are intracranial lesions located elsewhere. A magnetic resonance imaging needs to be obtained to appropriately investigate for these possibilities. Exertional headache, such as with exercise or during sexual activity, may represent a benign process such as migraine. However, if the headache is severe or thunderclap in onset, investigations will be necessary as already outlined above.

- **Headaches of new onset after the age of 50 years:**

The large majority of individuals who are destined to develop a primary headache disorder do so prior to age 50 years. Of course, this is not universal, and migraine or other primary headache disorders may begin even at an advanced age. Nevertheless, care should be taken before a diagnosis of a primary headache disorder is assigned. Many patients who do have the onset of a new headache disorder after age 50 years will merit brain imaging. In addition, after the age of 50 years, a new headache disorder should evoke suspicion of possible giant cell arteritis. Obviously, symptoms of polymyalgia rheumatica, jaw claudication, scalp tenderness or fever will increase the likelihood of this diagnosis. Findings of firm, nodular temporal arteries and decreased temporal pulses will increase the suspicion, as will an elevated sedimentation rate.

- **Symptoms suggestive of a systemic disorder such as fever, myalgias, weight loss or scalp tenderness or a known systemic disorder such as cancer or immune deficiency:**

Systemic disorders, while not incompatible with a coexistent primary headache disorder, should signal caution. Patients should be carefully evaluated. Obviously, the differential diagnosis will be long, and the index of suspicion for any given process will largely depend on the clinical setting.

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## Algorithm Annotations

- **Presence of subtle neurological signs suggests a secondary cause for headache. For example, meningismus, confusion, altered level of consciousness, memory impairment, papilledema, visual field defect, cranial nerve abnormalities, pronator drift, extremity weakness, significant sensory deficits, reflex asymmetry, extensor plantar response, or gait disturbance when accompanying a headache should elicit caution:**

While neurological signs may be unrelated to a headache, previously undocumented neurological findings that are presumably new need to be carefully considered. Usually cranial imaging will be the initial study. Depending on the index of suspicion, lumbar puncture and blood studies may be indicated.

- **Seizures:**

While seizures can occasionally be a manifestation of a primary headache disorder such as migraine, this is the exception and not the rule; it is a diagnosis of exclusion. Other etiologies for seizures including space-occupying lesions, infection, stroke and metabolic derangements will need to be considered. Again, magnetic resonance imaging is the imaging procedure of choice unless there is an issue of acute head trauma, in which case a computed tomography head scan should be obtained initially.

- **Diagnosis to be included in secondary headache:**

- |                                      |                                    |
|--------------------------------------|------------------------------------|
| - subdural hematoma                  | - giant cell arteritis             |
| - epidural hematoma                  | - acute hydrocephalus              |
| - tumor                              | - obstructive hydrocephalus        |
| - other metabolic disorders          | - cerebral spinal fluid leaks      |
| - craniocervical arterial dissection | - cerebral venous sinus thrombosis |

This list is not intended to be all-inclusive but rather to represent the most commonly seen diagnosis for secondary headache by the primary care clinician.

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## 14. Meets Criteria for Primary Headache Disorder?

The International Classification of Headache Disorders, second edition (ICHD-II) system for migraine has been studied in a community population sample without consideration of treatment. Findings suggest that the best criteria differentiating migraine from other headache types are the presence of nausea and/or vomiting in combination with two of the following three symptoms: photophobia, phonophobia and osmophobia (*Olesen, 2006 [Reference]*).

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**Modified Diagnostic Criteria**

<b>Episodic Headaches</b>	
<p><b>Migraine: with and without Aura</b></p> <p>A. At least two of 1-4, plus one of 5 or 6:</p> <ol style="list-style-type: none"> <li>1. Unilateral location</li> <li>2. Pulsating/throbbing quality</li> <li>3. Moderate or severe intensity (inhibits or prohibits daily activities)</li> <li>4. Aggravation by routine activity</li> <li>5. Nausea and/or vomiting</li> <li>6. Photophobia and phonophobia</li> </ol> <p>B. Aura criteria</p> <ol style="list-style-type: none"> <li>1. One or more fully reversible aura symptoms</li> <li>2. At least one aura symptom develops over more than 4 minutes or two or more symptoms occur in succession</li> <li>3. Symptoms do not last more than 60 minutes</li> <li>4. Attack follows within 60 minutes</li> </ol> <p>C. Previous similar attacks</p> <p>D. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.</p>	<p><b>Episodic Tension-Type Headache</b></p> <p>A. Headache less than 15 days per month.</p> <p>B. Lasts 30 minutes to 7 days</p> <p>C. At least two of the following characteristics:</p> <ol style="list-style-type: none"> <li>1. Pressing/tightening (non-pulsating) quality</li> <li>2. Mild to moderate intensity (may inhibit, but does not prohibit activities)</li> <li>3. Bilateral location</li> <li>4. Not aggravated by routine physical activity</li> </ol> <p>D. Both of the following:</p> <ol style="list-style-type: none"> <li>1. No nausea or vomiting (anorexia may occur)</li> <li>2. Photophobia and phonophobia are absent, or only one of the two is present</li> </ol> <p>E. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.</p>
<p><b>Cluster Headache</b></p> <p>A. Severe unilateral orbital, supraorbital and/or temporal pain lasting 15 to 180 minutes untreated</p> <p>B. Attack is associated with at least one of the following signs on the side of the pain:</p> <ol style="list-style-type: none"> <li>1. Conjunctival injection</li> <li>2. Lacrimation</li> <li>3. Nasal congestion</li> <li>4. Rhinorrhea</li> <li>5. Forehead and facial swelling</li> <li>6. Miosis</li> <li>7. Ptosis</li> <li>8. Eyelid edema</li> <li>9. Agitation, unable to lie down</li> </ol> <p>C. Frequency from one every other day to eight per day</p> <p>D. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.</p>	

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<b>Chronic Headaches</b>	
<p><b>Chronic Migraine</b></p> <p>A. Headache (tension type and/or migraine) on greater than or equal to 15 days per month for at least three months*</p> <p>B. Occurring in a patient who has had at least five attacks fulfilling criteria for 1.1 Migraine without aura</p> <p>C. On greater than or equal to eight days per month for at least three months headache has fulfilled C1 and/or C2 below, that is, has fulfilled criteria for pain and associated symptoms of migraine without aura</p> <ol style="list-style-type: none"> <li>1. Has at least two of a-d               <ol style="list-style-type: none"> <li>(a) unilateral location</li> <li>(b) pulsating quality</li> <li>(c) moderate or severe pain intensity</li> <li>(d) aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)</li> </ol> <p>and at least one of a or b</p> <ol style="list-style-type: none"> <li>(a) nausea and/or vomiting</li> <li>(b) photophobia and phonophobia</li> </ol> </li> <li>2. Treated and relieved by triptan(s) or ergot before the expected development of C1 above</li> </ol> <p>D. No medication overuse and not attributed to another causative disorder</p> <p><small>*Characterization of frequently recurring headache generally requires a headache diary to record information on pain and associated symptoms day by day for at least one month. Sample diaries are available at <a href="http://www.headache.org/for_Professionals/Headache_Dairy">http://www.headache.org/for_Professionals/Headache_Dairy</a>.</small></p>	<p><b>Chronic Tension-Type Headache</b></p> <p>A. Average frequency of greater than 15 attacks per month</p> <p>B. At least two of the following pain characteristics:</p> <ol style="list-style-type: none"> <li>1. Pressing/tightening quality</li> <li>2. Mild to moderate intensity (may inhibit, but does not prohibit activities)</li> <li>3. Bilateral location</li> <li>4. Not aggravated by routine physical activity</li> </ol> <p>C. Both of the following:</p> <ol style="list-style-type: none"> <li>1. No vomiting</li> <li>2. No more than one of the following: nausea, photophobia or phonophobia</li> </ol> <p>D. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.</p>
<p><b>Medication Overuse Headache</b></p> <p>A. Headache greater than or equal to 15 days/month</p> <p>B. Regular overuse for greater than three months of one or more acute/symptomatic treatment drugs as defined under one or more treatment drugs as noted below:</p> <ol style="list-style-type: none"> <li>1. Ergotamine, triptans, opioids or combination analgesic medications on greater than or equal to 10 days/month on a regular basis for greater than three months</li> <li>2. Simple analgesic or any combination of ergotamine, triptans, analgesic opioids on greater than or equal to 15 days/month on a regular basis for greater than three months without overuse of any single class alone</li> </ol> <p>C. Headache has developed or markedly worsened during medication overuse</p>	<p><b>Hemicrania Continua</b></p> <p>A. Headache for more than three months fulfilling criteria B-D</p> <p>B. All of the following characteristics:</p> <ul style="list-style-type: none"> <li>• unilateral pain without side-shift</li> <li>• daily and continuous, without pain-free periods</li> <li>• moderate intensity, but with exacerbations of severe pain</li> </ul> <p>C. At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain:</p> <ul style="list-style-type: none"> <li>• conjunctival injection and/or lacrimation</li> <li>• nasal congestion and/or rhinorrhoea</li> <li>• ptosis and/or miosis</li> </ul> <p>D. Complete response to therapeutic doses of indomethacin</p> <p>E. Not attributed to another disorder</p>

The table "Modified Diagnostic Criteria" has been modified from the International Classification of Headache Disorders, second edition (ICHD-II) system criteria and describes the differentiating criteria applicable for the diagnosis of migraine and other primary headache disorders.

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## 15. Evaluate Type of Primary Headache. Initiate Patient Education and Lifestyle Management

### Recommendations:

- Clinicians should provide patient education and lifestyle management options to patients with headache.
- Clinicians should instruct patients with headache to maintain a diary to clarify the frequency, severity, triggers and treatment responses to their headaches.

Migraine-associated symptoms are often misdiagnosed as "sinus headache" by patients and clinicians. This has led to the under diagnosis and treatment of migraine.

While education is of paramount importance in managing any condition, it is especially important in the ongoing management of headache. Patients may have to make lifestyle changes, are often required to make self-management choices in the treatment of individual headaches, and should maintain a diary to clarify the frequency, severity, triggers and treatment responses. Most patients should be educated on the following:

- Headache is due to physiologic disorders, to which individuals may be genetically predisposed.
- Identifiable food or alcohol triggers are present in a minority of patients.
- Most patients will benefit from stress reduction, regular eating and sleeping schedules, and regular aerobic exercise.
- Chronic daily headache, including transformed migraine, is associated with overuse of analgesics or acute treatment drugs. Use of NSAIDs for acute treatment of headache for more than nine days per month or use of aspirin more than 15 days is associated with an increased risk of chronic daily headaches.
- Keeping a headache diary has the potential benefit of monitoring treatment effect upon severity, frequency and disability.
- Acute treatment has the goal of shortening individual headaches, while prophylaxis can reduce frequency and possibly severity.
- It is often not possible to eliminate primary headache completely.

The presentation of four clinical characteristics and duration can help clinicians determine if the migraine headache is likely, possible or unlikely by using the simple mnemonic POUNDing (Pulsatile quality; duration of 4 to 72 hours; Unilateral location; Nausea or vomiting; Disabling intensity) for the screening of migraine headache (*Detsky, 2006 [Decision Analysis]*). See the table, "[Modified Diagnostic Criteria](#)" for more information.

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## 19. Chronic Daily Headache

Chronic daily headache refers to the presence of a headache more than 15 days per month for greater than three months. Chronic daily headache is not a diagnosis but a category that may be due to disorders representing primary and secondary headaches. Secondary headaches are typically excluded with appropriate neuroimaging and other tests. Chronic daily headache can be divided into those headaches that occur nearly daily that last four hours or less and those that last more than four hours, which is more common. The shorter-duration daily headache contains less-common disorders such as chronic cluster headache and other trigeminal autonomic cephalgias. Only daily headaches of long duration are considered here.

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Chronic daily headache has been estimated to occur in 2.5-4% of the general population with surveys showing that chronic tension-type headache is a bit more common than chronic migraine (transformed migraine). In the clinic setting, chronic migraine is much more common than chronic tension-type headache. As with migraine, chronic daily headaches are more common in women than men. An associated factor for chronic daily headache is medication overuse. As outlined below, the Headache Classification Committee of the International Classification of Headache Disorders, second edition (ICHD-II) has provided revised guidelines for chronic migraine and medication overuse headache (*Olesen, 2006 [Low Quality Evidence]*).

In diary studies, patients who fulfill criteria for a diagnosis of the older definition of transformed migraine also fulfill criteria for a diagnosis of the revised definition of chronic migraine, which is presented below (*Liebenstein, 2007 [Low Quality Evidence]*; *Bigal, 2006 [Low Quality Evidence]*).

Please see the [Modified Diagnostic Criteria](#) table for the revised International Classification of Headache Disorders, second edition (ICHD II) criteria for chronic migraine.

### **Medication-overuse headache**

When medication overuse is present, this is the most likely cause of chronic headache. However, if the acute headache relieving medications are discontinued for an extended period (often two months) and the headache symptoms persist, it is likely chronic headache, not medication overuse type headache, even though the ICHD-II criteria do not require this for the diagnosis of medication overuse.

Please see the [Modified Diagnostic Criteria](#) table for the International Classification of Headache Disorders, second edition (ICHD-II), system revised criteria for medication-overuse headache.

### **Chronic Tension-Type Headache**

As noted, chronic tension-type headache is much less common than episodic-type headache; it is more likely seen in clinical practice. Please see the [Modified Diagnostic Criteria](#) table for the International Classification of Headache Disorders, second edition (ICHD-II) criteria for chronic tension-type headache.

### **Hemicrania Continua**

A less common but not rare (and under recognized) cause for chronic daily headache is hemicrania continua. Hemicrania continua description is a persistent, strictly unilateral headache responsive to indomethacin. Please see the [Modified Diagnostic Criteria](#) table for the International Classification of Headache Disorders, second edition (ICHD-II) criteria for hemicrania continua.

A much rarer disorder is that known as new daily persistent headache. This disorder is characterized by its sudden onset, with the patient often able to note the date and time it began. There is no history of prior significant headaches. It is typically bilateral and usually resembles migraine or tension-type headache. Some individuals report an antecedent viral infection.

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## **20. Other Headache**

Other headaches include cervicogenic and persistent daily headaches.

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## **21. Specialty Consultation Indicated?**

### **Recommendation:**

- Clinicians may consider specialty consultation when the diagnosis or etiology cannot be confirmed, warning signals exist or quality of life is impaired.

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The decision to seek a specialty consultation will depend upon the practitioner's familiarity and comfort with headache and its management. Specialty consultation may be considered when:

- The diagnosis cannot be confirmed
- Etiology cannot be diagnosed or warning signals are present
- Headache attacks are occurring with a frequency or duration sufficient to impair the patient's quality of life despite treatment or the patient has failed to respond to the acute remedies, or is in status migrainosus

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## **22. Perform Diagnostic Testing If Indicated**

### **Recommendation:**

- Clinicians should use a detailed headache history, that includes duration of attacks and the exclusion of secondary causes, as the principal means to diagnose primary headache. Additional testing in patients without atypical symptoms or an abnormal neurologic examination is unlikely to be helpful.

There are, as yet, no tests that confirm the diagnosis of primary headache. The diagnosis of primary headache is dependent on the clinician. The work group recommends careful consideration before proceeding with neuroimaging (computed tomography or magnetic resonance imaging). It is uncommon for neuroimaging to detect an abnormality in persistent headaches of longer duration versus new onset situations. Selective testing including neuroimaging or electroencephalogram, lumbar puncture, cerebrospinal fluid and blood studies may be indicated to evaluate for secondary headache if causes of concern have been identified in the patient history or physical examination. (See [Annotation #12, "Causes for Concern?"](#)) Diagnosis may be complicated if several headache types coexist in the same patient. The following symptoms significantly increased the odds of finding a significant abnormality on neuroimaging in patients with non-acute headache:

- Rapidly increasing headache frequency
- History of lack of coordination
- History of localized neurologic signs or a history such as subjective numbness or tingling
- History of headache causing awakening from sleep (although this can occur with migraine and cluster headache) (*Silberstein, 2000a [Guideline]*).

In a study of 750 patients questioned, 47% had throbbing quality of headaches, while another study showed 30% of 1,000 cases of tension headache patients had pulsatile quality pain, 40% of all patients with migraine have bilateral headaches. Duration of an attack is important. It is felt that pitfalls in interpreting diagnostic criteria may lie in how questions are asked (*Blau, 1993 [Low Quality Evidence]*).

There is difficulty in developing an operational system to diagnose headaches with the lack of objective diagnostic tests that identify various types of headache disorders absolutely. International Classification of Headache Disorders, second edition (ICHD-II) criteria depend largely on a detailed headache history and the exclusion of secondary cause for headache through a physical and neurological examination. Concern of a secondary cause for headache may necessitate testing or further evaluation (*Olesen, 1994 [Guideline]*).

A total of 897 computed tomography scans or magnetic resonance images were done on migraine patients with findings of three tumors and two arteriovenous malformations. At this time, there is evidence to define the role of computed tomography and magnetic resonance imaging in the evaluation of headache patients. 1,800 computerized tomographic scans and magnetic resonance studies done on patients with headaches, including those that were acute, progressively worsening, and chronic, found only 2.4% of those imaged

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had arteriovenous malformation, aneurysms, subdural hematoma or hydrocephalus was found (*American Academy of Neurology Quality Standards Subcommittee, 1994 [Guideline]*).

In a retrospective study, 592 patients with headaches and normal neurological exam were examined by computed tomography scanning between 1990 and 1993 at a cost of \$1,000 per scan. None of the patients had any serious intracranial pathology identified. This technique is costly and unrewarding (*Akpek, 1995 [Cost-analysis]*).

In a case series study 52 migraineurs were evaluated by spinal taps, cerebral spinal fluid analysis and tap pressure. Pressures of cerebral spinal fluid and the chemistry evaluation of the same bore no direct relationship to the presence of headache diagnosis (*Kovács, 1989 [Low Quality Evidence]*).

A summary statement reviewed articles from 1941 to 1994 with no study of electroencephalograms improving diagnostic accuracy for the headache sufferer. Electroencephalography does not delineate subtypes or screen for structural causes of headache effectively (*American Academy of Neurology Quality Standards Subcommittee, 1994 [Guideline]*). In the absence of studies showing improved diagnostics with electroencephalogram, there is no indication for routine use of electroencephalograms in the diagnosis of headache.

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## **23. Findings Consistent with Secondary Headache?**

If diagnostic evaluation leads to a diagnosis other than primary headache, subsequent care of the patient would fall beyond the scope of this guideline.

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## **Migraine Treatment Algorithm Annotations**

### **27. Patient Meets Criteria for Migraine**

Migraine is the most common headache disorder seen by primary care clinicians.

It is expected that a patient with headache will undergo a diagnostic workup (see the [Diagnosis Algorithm](#)) establishing the diagnosis of migraine before initiating acute treatment.

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### **28. Is Patient Experiencing a Typical Headache?**

Each individual headache must be evaluated in the context of the patient's prior migraine headaches. The practitioner must always remain alert to the possibility of secondary causes for headache, particularly when there is a previously established history of a primary headache disorder such as migraine.

Migraine headache does not preclude the presence of underlying pathology (arterial dissection, intracranial aneurysm, venous sinus thrombosis, ischemic or hemorrhagic stroke, temporal arteritis, etc.) that may also present with "vascular headaches." If the history is scrutinized, ominous causes for headaches can often be identified and treated with the potential to avoid catastrophe.

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### **30. Categorize According to Peak Severity Based on Functional Impairment, Duration of Symptoms, and Time to Peak Impairment**

#### **Recommendations:**

- Clinicians should categorize headache according to peak severity, duration of symptoms and time to peak impairment.
- Clinicians should treat according to severity.

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**Algorithm Annotations**

Accurate categorization and characterization by both clinicians and patients is important. The categorization of migraine influences choice of treatment method.

**Severity levels:**

**Mild** Patient is aware of a headache but is able to continue daily routine with minimal alteration.

**Moderate** The headache inhibits daily activities but is not incapacitating.

**Severe** The headache is incapacitating.

**Status** A severe headache that has lasted more than 72 hours.

There may be additional features that influence choice of treatment. For example, parenteral administration (subcutaneous, nasal) should strongly be considered for people whose time to peak disability is less than one hour, who awaken with headache, and for those with severe nausea and vomiting.

Determining functional limitations during migraine episodes is the key to determining the severity and therefore the best treatment for a patient. Clinicians and patients should stratify treatment based on severity rather than using stepped care, though patients will often use stepped care within an attack. This algorithm uses a stratified-care model.

**Factors That May Trigger Migraine**

Certain influences can lead to a migraine attack. It is important to note that although a single trigger may provoke the onset of a migraine, a combination of factors is much more likely to set off an attack.

**Environmental:**

- Temperature (exposure to heat/cold)
- Head or neck injury
- Odors (smoke, perfume)
- Bright lights or glare
- Weather changes
- Flying/high altitude
- Noise
- Motion
- Physical strain

**Lifestyle Habits:**

- Chronic high levels of stress
- Disturbed sleep patterns
- Skipping meals and/or poor diet
- Smoking

**Hormonal:**

- Puberty
- Menstruation or ovulation
- Using oral contraceptives or estrogen therapy
- Menopause
- Pregnancy

**Emotional:**

- Anxiety
- Anger (including repressed anger)
- "Let-down" response
- Depression
- Excitement or exhilaration

**Medications:**

- Nitroglycerin
- Oral contraceptives
- Nifedipine
- Hormone therapy

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**Dietary:**

Dietary triggers vary considerably from patient to patient, are overall a minor and infrequent trigger for migraine headaches, and will not consistently precipitate a migraine headache in an individual for whom they have been a trigger in the past.

- Citrus fruit
- Caffeine
- Chocolate
- Foods containing nitrites
- Aspartame
- Aged cheese
- Alcohol (red wine, beer)
- Foods containing monosodium glutamate

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**32. Mild Treatment****Recommendations:**

- Clinicians may manage mild migraines with over-the-counter medications.
- Clinicians may use triptans for mild migraine pain levels.

The guideline work group presumes most mild migraine headaches will be managed by self-care, which implies an emphasis on over-the-counter medications. However, since only 2-12% of initially mild migraine episodes remain mild (with the remainder progressing), treatments effective for mild headaches may be useful for only a short time. Studies on treatment of migraine headache at the mild level show that triptans are more effective in abolishing pain at this stage than if the headache is more severe. It is acceptable to use other symptomatic headache relief drugs, as well as triptans, for mild headache. However, current retrospective analyses of mild pain treatment studies reveal triptan response to two-hour pain freedom to be superior to any other comparator drug. Please see [Appendix A, "Drug Treatment for Headache,"](#) and [Appendix B, "Drug Treatment for Adjunctive Therapy."](#)

Use of NSAIDs for acute treatment of headache for more than nine days per month or use of aspirin for more than 15 days is associated with an increased risk of chronic daily headache.

Early treatment of migraines with effective medications improves a variety of outcomes including duration, severity and associated disability (*Valade, 2009 [Meta-analysis]*).

Given a longer half-life of naratriptan, headache response is delayed with naratriptan when compared with other selective 5-hydroxy tryptamine (5-HT) receptor agonists. However, headache recurrence may be less frequent.

Second doses of triptans have not been shown to relieve headache more if the first dose has been ineffective.

Studies show that sumatriptan and naproxen sodium in combination may be more effective than either drug alone. However, there are no studies that demonstrate that sumatriptan 85 mg/naproxen sodium 500 mg is more effective than sumatriptan and naproxen sodium taken together. Therefore, a dose of sumatriptan 100 mg and a dose of naproxen sodium 550 mg taken at the same time is recommended.

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**33. Successful?**

Success for treatment of migraine is defined as complete pain relief and return to normal function within two hours of taking medication. In addition, patients should not have intolerable side effects and should find their medications reliable enough to plan daily activities despite migraine headache (*Dowson, 2004a [Low Quality Evidence]; Dowson, 2004b [Low Quality Evidence]*).

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## Algorithm Annotations

Consider reasons for treatment failure and change treatment plan.

Common reasons for migraine treatment failure:

- Acute medication or analgesic overuse
- Medication dose too little or used too late
- Inadequate medication for degree of disability. Medication not well matched with most disabling symptoms (e.g., using oral agents for a patient with vomiting) or inappropriate route of administration (e.g., using oral agents for a headache where maximum disability occurs quickly)
- Failure to use adjunctive medication (e.g., caffeine, antiemetics)
- Inaccurate diagnosis

Patient adherence to therapy contributes to reaching treatment goals. The clinician-patient relationship plays a key role in improving adherence. Clinicians should ask patients open-ended, non-threatening questions regularly to assess adherence. Questions that probe for factors that contribute to non-adherence could include those surrounding adverse reactions, misunderstandings of treatment, depression, cognitive impairment, complex regimens and financial constraints.

Interventions to improve adherence include simplification of the drug regimen (frequency and complexity); use of reminder systems; involvement of family or friends; a health care team approach including nurses, pharmacists, and educators in addition to clinicians; written instructions; and educating the patient about potential adverse effects, importance of therapy, and realistic treatment goals.

For example:

- A. Assess the patient's knowledge of the condition and expectations for treatment:

"What is/will be the most difficult task for you in reaching your treatment goal?"

- B. Assess the patient's medication administration process:

"How do you remember to take your medication each day? Do you use a reminder device such as a pill box or alarm?"

- C. Assess the patient's barriers to adherence:

"Do you have a difficult time opening medication bottles, swallowing pills or reading small print on labels?"

"Are you comfortable with your ability to follow the treatment plan that we have designed together?"

"Are you experiencing any unusual symptoms that you think may be due to your medication?"

*(Nichols-English, 2000 [Low Quality Evidence])*

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## 36. Moderate Treatment

### Recommendation:

- Clinicians should avoid the use of opiates and barbiturates in the treatment of headache.

Early treatment of migraines with effective medications improves a variety of outcomes including duration, severity, and associated disability (*Valade, 2009 [Meta-analysis]*).

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The use of opiates and barbiturates should be avoided. This guideline emphasizes the use of other agents over opiates and barbiturates, recognizing that many migraineurs are currently treated with drugs from the latter two classes. In general, opiates are characterized by having a short pain-relief window, release inflammatory neurochemicals, and increase vasodilation; none of these addresses the currently known treatment issues and pathophysiology of migraine.

Meperidine should be avoided. The metabolite of meperidine, normeperidine, has a long half-life and produces less analgesic effect, and there is an increased risk of seizures that cannot be reversed by naloxone. We have specifically excluded butorphanol because of its high potential for abuse and adverse side-effect profile.

If an opiate must be used, meperidine should not be the opiate selected.

See [Appendix A, "Drug Treatment for Headache."](#)

See [Appendix B, "Drug Treatment for Adjunctive Therapy."](#)

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### 37. Successful?

See [Annotation #33](#) for information.

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### 42. Consultation with Headache Specialist

A headache specialist is a practitioner, often but not always, a neurologist who has extensive experience, knowledge of, and demonstrated high standards of health care in the field of headache. There are advanced training programs in headache medicine.

The American Headache Society has a membership directory of practitioners interested in the field of headache and can be contacted if the name of a recommended specialist in a particular geographic location is required. (American Headache Society can be reached by e-mail at [AHSHQ@talley.com](mailto:AHSHQ@talley.com). The Web site: <http://www.americanheadachesociety.org>)

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### 43. Status (Greater Than 72 Hour Duration)

#### Recommendation:

- It is recommended that the patient be hydrated prior to neuroleptic administration with 250-500 mL of 5% dextrose with 0.45% sodium chloride intravenously and advised of the potential for orthostatic hypotension and acute extrapyramidal side effects. The patient should be observed in a medical setting as clinically appropriate after administration of a neuroleptic and should not drive for 24 hours.

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### 44. Adjunctive Therapy

#### Recommendation:

- Clinicians may consider adjunctive therapy as a treatment option for headache.

See [Appendix B, "Drug Treatment for Adjunctive Therapy."](#) As adjunctive therapy, any of the listed medications can be used singularly or in compatible combination. For intermittent, infrequent headache, caffeine should be added as first choice when not contraindicated. The use of caffeine in patients with chronic

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daily headache is to be discouraged. The prokinetic agent metoclopramide could be considered next. This guideline has no other preferences.

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## 45. Patient Meets Criteria for Dihydroergotamine Mesylate (DHE)?

Dihydroergotamine mesylate is effective in halting intractable migraine attacks or migraine status. Dihydroergotamine mesylate is also effective in halting the acute cycle of cluster headaches.

Dihydroergotamine mesylate must not be given to patients with the following conditions:

- Pregnancy and breastfeeding
- History of ischemic heart disease
- History of Prinzmetal's angina
- Severe peripheral vascular disease
- Onset of chest pain following administration of test dose
- Within 24 hours of receiving any triptan or ergot derivative
- Elevated blood pressure
- Patients with hemiplegic or basilar-type migraine \*
- Cerebrovascular disease

\* Basilar-type migraine is defined as three of the following features: diplopia, dysarthria, tinnitus, vertigo, transient hearing loss or mental confusion (*Headache Classification Subcommittee of the International Headache Society, 2004 [Guideline]*).

Intravenous dihydroergotamine mesylate is the method most frequently employed to terminate a truly intractable migraine attack or migraine status. The protocol outlined in the dihydroergotamine mesylate algorithm is effective in eliminating an intractable migraine headache in up to 90% of patients within 48 hours. This method of administration has also been found to be effective in terminating an acute cycle of cluster headaches, as well as chronic daily headaches with or without analgesic/ergotamine rebound.

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## 47. Chlorpromazine, Intravenous Valproate Sodium, Intravenous Magnesium Sulfate or Prochlorperazine

### Recommendations:

- Clinicians should treat patients with migraine > 72 hours who do not meet criteria for DHE, with chlorpromazine, intravenous valproate sodium, intravenous magnesium sulfate or prochlorperazine.
- Clinicians should premedicate patients with diphenhydramine or benztropine who have migraine for > 72 hours, who do not meet criteria for DHE and who have a history of dystonic reaction.

See Appendix A, "Drug Treatment for Headache," and Appendix B, "Drug Treatment for Adjunctive Therapy."

If chlorpromazine, valproate sodium or intravenous magnesium sulfate was used previously, one may not wish to repeat.

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## 48. Successful?

See [Annotation #33](#) for more information.

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## 49. Opiates

These are not drugs of first choice, and headache practice recommends against the use of meperidine. Nor-meperidine, the active metabolite of meperidine, has a long half-life and is neuroexcitatory and neurotoxic. There is inconsistent absorption of opiates, at least with meperidine, when injected intramuscularly, and they are less effective than when given intravenously. Opiates release inflammatory neurochemicals and increase vasodilation that are mechanistically counterproductive to currently known migraine pathophysiology and can exacerbate headaches. Studies have been done using meperidine, but the effects are likely due to class effect, and other opiates are likely to be just as effective (*Duarte, 1992 [High Quality Evidence]*). However, it should be noted that there are no studies to support opiate effectiveness.

See [Appendix A, "Drug Treatment for Headache,"](#) and [Appendix B, "Drug Treatment for Adjunctive Therapy."](#)

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## 51. Dexamethasone

See [Appendix A, "Drug Treatment for Headache,"](#) and [Appendix B, "Drug Treatment for Adjunctive Therapy."](#)

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## Migraine Treatment – Annotations #32, 36, 39, 44, 47, 49, 51

### Adolescents

At this time the majority of the adolescent literature supports a strong placebo effect in this age group. Success of triptans and prophylactic medications in patients age 12-17 yield similar positive outcomes as in adult studies, but placebo administered in blinded, controlled studies has a similar effect. There has been a recent study that supports the use of almotriptan with statistically significant efficacy over placebo. As an acute treatment, almotriptan in the dose of 12.5 mg was effective in relieving pain and associated symptoms and was well tolerated (*Linder, 2008 [High Quality Evidence]*).

Refer to [Appendix A, "Drug Treatment for Headache,"](#) for more information.

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## Tension-Type Headache Algorithm Annotations

### 59. Patient Meets Criteria for Tension-Type Headache?

Tension-type headache is one of the most common primary headaches. See [Annotation #14, "Meets Criteria for Primary Headache Disorder?"](#) for episodic (less than 15 days per month) and chronic tension-type headache (more than 15 days per month).

It is important to evaluate the patient who comes to the office for tension-type headache for the possibility of migraine. While the International Classification of Headache Disorders, second edition (ICHD-II) system suggests migraine and tension-type headaches are distinct disorders, there is evidence to suggest that for the migraineur, tension-type headache is actually a low-intensity migraine.

(*Torelli, 2004 [High Quality Evidence]*; *Ashina, 2003 [Low Quality Evidence]*; *Zhao, 2003 [Low Quality Evidence]*)

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## 62. Acute Treatment

### Recommendation:

- Clinicians may utilize over-the-counter analgesics or prescription NSAIDs for tension-type headache treatment.

Analgesics offer a simple and immediate relief for tension-type headache. Medication overuse is potentially a concern that can lead to chronic daily headache. Use of drugs for acute treatment of headache for more than nine days per month is associated with an increased risk of chronic daily headache.

See [Appendix A, "Drug Treatment for Headache,"](#) and [Appendix B, "Drug Treatment for Adjunctive Therapy."](#) (Torelli, 2004 [High Quality Evidence]; Ashina, 2003 [Low Quality Evidence]; Zhao, 2003 [Low Quality Evidence])

Electromyography biofeedback has been found to have an effect on tension-type headaches. The goal is to help patients recognize muscle tension. Fifty-three studies have shown medium to large effect (Bendtsen, 2010 [Guideline]).

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## 66. Prophylactic Treatment

### Recommendation:

- Prophylactic treatment, including the use of tricyclic antidepressants, may be used for chronic tension-type headaches.

Prophylactic therapy is reserved for patients with chronic tension-type headache (more than 15 headaches per month).

Tricyclic antidepressants are effective in reducing the frequency and severity of tension-type headache.

(Torelli, 2004 [High Quality Evidence]; Ashina, 2003 [Low Quality Evidence]; Zhao, 2003 [Low Quality Evidence])

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## Cluster Headache Algorithm Annotations

### 71. Patient Meets Criteria for Cluster Headache?

There is no more severe pain than that sustained by a cluster headache sufferer. This headache is often termed "suicide headache." Cluster headache is characterized by repeated short-lasting but excruciating intense attacks of strictly unilateral peri-orbital pain associated with local autonomic symptoms or signs. The most striking feature of cluster headache is the unmistakable circadian and circannual periodicity. Many patients typically suffer daily (or nightly) from one or more attacks over a period of weeks or months.

(Dodick, 2000 [Low Quality Evidence]; Goadsby, 1997 [Low Quality Evidence]; Lipton, 1998 [High Quality Evidence])

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### 75. Acute Treatment

#### Recommendations:

- Clinicians should utilize inhaled oxygen for the treatment of cluster headaches at a rate of 7-15 L/min.

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- Clinicians should consider using subcutaneous sumatriptan or intranasal zolmitriptan as a first line option for the treatment of cluster headaches.

Oxygen inhalation is highly effective when delivered at the beginning of an attack with a non-rebreathing facial mask (7-15 L/min). Most patients will obtain relief within 15 minutes. Acute drugs may be difficult to obtain in adequate quantity.

Subcutaneous sumatriptan and intranasal zolmitriptan are the most effective self-administered medication for the relief of cluster headaches. Sumatriptan is not effective when used before the actual attack nor is it useful as a prophylactic medication (*Law, 2010 [Systematic Review]*). Intranasal sumatriptan can also be considered for acute treatment (*Francis, 2010 [Moderate Quality Evidence]*).

Dihydroergotamine mesylate provides prompt and effective relief from cluster headaches in 15 minutes, but due to the rapid peak intensity and short duration of cluster headaches, dihydroergotamine mesylate may be a less feasible option than sumatriptan.

See [Appendix A, "Drug Treatment for Headache,"](#) and [Appendix B, "Drug Treatment for Adjunctive Therapy."](#) (*Dodick, 2000 [Low Quality Evidence]*; *Goadsby, 1997 [Low Quality Evidence]*; *Lipton, 1998 [High Quality Evidence]*)

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## 76. Bridging Treatment

### Recommendation:

- Clinicians should initiate bridging treatment or transitional prophylaxis simultaneously with maintenance prophylactic treatment after acute treatment has suppressed the initial attack for cluster headaches.

Bridging treatment allows for the rapid suppression of cluster attacks in the interim until the maintenance treatment reaches therapeutic levels.

Options for bridging treatment are:

- Corticosteroids
- Occipital nerve block

(*Capobianco, 2006 [Guideline]*; *Husid, 2006 [Low Quality Evidence]*; *Sandrini, 2006 [Low Quality Evidence]*; *Ambrosini, 2005 [High Quality Evidence]*; *Peres, 2002 [Low Quality Evidence]*; *Dodick, 2000 [Low Quality Evidence]*)

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## 77. Maintenance Prophylaxis

### Recommendation:

- Clinicians should initiate maintenance prophylaxis to provide sustained suppression of cluster headaches over the expected cluster period.

Effective prevention cannot be overemphasized in these patients. Maintenance prophylaxis is critically important since cluster headache sufferers typically experience one or more daily (or nightly) attacks for a period of weeks or months. The goal of transitional therapy is to induce rapid suppression of attacks while maintenance prophylaxis is intended to provide sustained suppression over the expected cluster period.

If the patient has intractable headache or is unresponsive to prophylactic treatment, consider referral to a headache specialist.

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See Appendix A, "Drug Treatment for Headache," and Appendix B, "Drug Treatment for Adjunctive Therapy." (Dodick, 2000 [Low Quality Evidence]; Olesen, 1999 [Reference]; Goadsby, 1997 [Low Quality Evidence]; Lipton, 1998 [High Quality Evidence])

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## Dihydroergotamine Mesylate (DHE) Algorithm Annotations

### 84. Intravenous Metoclopramide 10 mg Intravenous

Metoclopramide (10 mg) is given either by direct intravenous injection over two-three minutes, or infused intravenously in 50 mL of normal saline over 15 minutes. Each dose of metoclopramide should be administered 15 minutes prior to each dihydroergotamine mesylate injection. Although uncommon, acute extrapyramidal side effects such as dystonia, akathisia, and oculogyric crisis may occur after administration of metoclopramide. Benztropine mesylate is effective in terminating this unusual adverse event, given as a 1 mg injection (intravenous or intramuscular). Often after five doses of metoclopramide, it may be given as needed every eight hours for nausea (Ellis, 1993 [High Quality Evidence]).

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### 85. Begin Continuous Dihydroergotamine Mesylate (DHE)

Begin dihydroergotamine mesylate 2 mg in 1,000 mL normal saline at 42 mL/hr. Limit the dose of DHE to no more than 2 mg/24 hours.

Continue intravenous metoclopramide 10 mg IV every eight hours as needed for nausea.

#### Side effects:

- If significant nausea occurs at any time, reduce the rate of dihydroergotamine mesylate to 21 to 30 mL/hr.
- If diarrhea occurs, give diphenoxylate with atropine, one or two tablets, three times daily as needed.
- If excessive anxiety, jitteriness (akathisia) or dystonic reaction occurs, give intravenous benztropine 1 mg.

It may be continued up to seven days. Opioid analgesics should not be used since these are likely to prolong the headache via analgesic rebound.

This is an adjusted Ford modification of the Raskin protocol. This is a continuous protocol as this is the preferred method. This approach is an alternative to the intermittent dosing of dihydroergotamine mesylate as outlined in the Raskin protocol, and some practitioners may prefer it rather than the intermittent dihydroergotamine mesylate protocol. Continuous dihydroergotamine mesylate, like the intermittent administration, can be continued for seven days, although 72 hours is more typical. Opioid analgesics should not be used with either protocol since these are likely to prolong the headache via analgesic rebound.

Ford, et al. described results of an open trial comparison between intermittent intravenous dihydroergotamine mesylate and continuous infusion dihydroergotamine mesylate. Success in treating migraine status was virtually the same with each protocol. The Ford variation may be preferred by some clinicians. This protocol should be used only with an intravenous pump (Ford, 1997 [Low Quality Evidence]; Queiroz, 1996 [Low Quality Evidence]; Raskin, 1986 [Low Quality Evidence]).

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## Menstrual-Associated Migraine Algorithm Annotations

### 87. Patient Meets Criteria for Menstrual-Only or Menstrual-Associated Migraine

#### Recommendation:

- Clinicians should advise women who meet criteria for menstrual-associated migraine to keep a continuous daily record of headache occurrence, severity, duration and menstrual flow for at least two months.

"Menstrual migraine," a term misused by both patients and clinicians, lacks precise definition. The International Classification of Headache Disorder, second edition (ICHS-II) system has proposed that menstrual-only migraine be defined as attacks exclusively starting two days before and first two days of the menstrual cycle (*Pringsheim, 2008 [Meta-analysis]; Headache Classification Subcommittee of the International Headache Society, 2004 [Guideline]*). The woman should be free from attacks at all other times of the cycle.

Many women who do not have attacks exclusively with menses are considered to have menstrual-associated migraines (*MacGregor, 1996 [Low Quality Evidence]*).

The clinician and patient need to discuss diary documentation. The patient should keep a continuous daily record for at least two months to include the following:

- Day/time of headache
- Duration
- Severity of headache
- Onset of menstrual flow

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### 91. Consider Cyclic Prophylaxis

#### Recommendation:

- Clinicians may consider non-hormonal cyclic prophylactic treatment with NSAIDs and triptans for patients with menstrual-associated migraine.
- Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs should be considered approaches of first choice in the prophylactic treatment of migraine associated with menses. Many clinicians consider triptans to be equally effective, but there are no comparative studies. [*Conclusion Grade III: See Conclusion Grading Worksheet A – Annotation #91 (Non-Steroidal Anti-Inflammatory Drugs)*]

Naproxen sodium has been used as a preventive agent, although other non-steroidal anti-inflammatory drugs may also be effective. Typically, the agent is initiated two to three days before anticipated onset of the headache and continued through the at-risk period.

Virtually every review paper supports the use of non-steroidal anti-inflammatory drugs for cyclic prophylaxis. There are almost no controlled studies in this setting, with two smaller studies supporting prophylaxis with naproxen sodium (*Boyle, 1999 [Low Quality Evidence]; Silberstein, 1999 [High Quality Evidence]; Kornstein, 1997 [Low Quality Evidence]*).

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- Triptans

There are good placebo studies supporting the use of triptans (sumatriptan, naratriptan, frovatriptan and zolmitriptan) for cyclic prophylaxis (*Tuchman, 2008 [High Quality Evidence]; Silberstein, 2000b [High Quality Evidence]; Newman, 1998 [Low Quality Evidence]*).

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## 94. Consider Hormone Prophylaxis

### Recommendation:

- Clinicians may consider hormone prophylaxis treatment for patients with menstrual-associated migraines.

- **Transdermal estradiol**

Estrogen levels decrease during the late luteal phase of the menstrual cycle, likely triggering migraine. Estrogen replacement prior to menstruation has been used to prevent migraine.

Estradiol patches, 50-100 mcg, are applied 48 hours prior to expected onset of migraine and used for one week.

The 50 mcg estradiol patch, applied 48 hours before anticipated onset of menses and continuing for seven days, was effective in relieving headaches in a subgroup of women with menstrual migraines confirmed by neurophysiological testing. Others have shown a better clinical outcome with 100 mcg estradiol patches than with lower dose patches. Oral estrogen has been less effective than transdermal estrogen in prophylaxis of menstrual migraine.

*(Becker, 1999 [Low Quality Evidence]; Cupini, 1995 [Low Quality Evidence]; Larsson-Cohn, 1970 [Low Quality Evidence])*

- **Estrogen-containing contraceptives**

Estrogen-containing contraceptives have a variable effect on migraines, causing worsening of headaches in some patients, improvement of headaches in a small percentage of patients, and no change in migraines in other patients. We are not aware of any population-based studies on this topic.

The effect of estrogen-containing contraceptives on migraines is unpredictable. In one study, migraines worsened in 39% of patients, improved in 3%, and remained unchanged in 39%. Another author reported improvement in migraines in 35% of patients when estrogen-containing contraceptives were started.

*(Becker, 1999 [Low Quality Evidence]; Cupini, 1995 [Low Quality Evidence]; Larsson-Cohn, 1970 [Low Quality Evidence])*

In a contraceptive containing drospirenone, an extended 168-day placebo-free oral contraceptive regimen showed a significant decrease in duration, severity of headaches and loss of function due to headache compared with a standard 21/7 oral contraceptive cycle (*Sulak, 2007 [Low Quality Evidence]*). In 2011, the Food and Drug Administration concluded that drospirenone may be associated with a higher risk for blood clots than other progestin-containing pills. <http://www.fda.gov/Drugs/DrugSafety/ucm273021.htm>.

- **GnRH agonists with "add back" therapy**

For patients with severe menstrual migraine unrelieved by other therapies, suppression of the menstrual cycle with a gonadotropin-releasing hormone agonist and "add back" therapy may be effective.

Suppression of ovarian steroid production followed by a constant estrogen-progestin milieu was studied in five women with severe menstrual migraine. All patients reported dramatic improvement in

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functioning and quality of life and a decrease in analgesic medications used for headache relief. Two patients discontinued therapy and had increased headache frequency. The monthly cost of GnRH agonist therapy is about 10 times the cost of conventional hormone therapy. GnRH agonists and "add back" therapy may also be associated with erratic bleeding. This therapy should probably be managed by a gynecologist or endocrinologist in concert with a headache specialist.

Tamoxifen, danazol and bromocriptine have shown limited efficacy in treatment of menstrual migraine.

Whether oophorectomy is an effective treatment for refractory migraines is not settled at this time.

(Herzog, 1997 [Low Quality Evidence]; Murray, 1997 [Low Quality Evidence]; Lichten, 1991 [Low Quality Evidence]; O'Dea, 1990 [Low Quality Evidence])

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## Perimenopausal or Menopausal Migraine Algorithm Annotations

### 98. Perimenopausal or Menopausal with Active Migraine History and Is a Potential Candidate for Hormone Therapy

#### Recommendation:

- Clinicians should not prescribe hormone therapy for perimenopausal or menopausal migraine treatment in patients who are pregnant or have unexplained bleeding.

Menopause is the permanent cessation of menses.

Perimenopause is the span of time from the reproductive to the post-reproductive interval.

Hormone therapy may worsen, improve or leave migraines unchanged.

In a study of 112 women taking hormone therapy, 52 reported worsening of migraines, 50 reported improvement, and 10 reported no change in migraine headaches. More women improved with transdermal than oral estrogen (Wang, 2003 [Low Quality Evidence]; Nappi, 2001 [High Quality Evidence]; MacGregor, 1997 [Low Quality Evidence]).

#### Women with these conditions are not candidates for hormone therapy:

- Pregnancy or unexplained bleeding: these are temporary but absolute contraindications to hormone therapy.
- Past history of breast cancer or endometrial cancer: while usually considered contraindications to hormone therapy, short-term use for severe menopausal symptoms may be considered with proper precautions.

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### 103. Hormone Therapy

- Transdermal, transvaginal or oral estrogen
- Progestin if indicated
- Estrogen-containing contraceptives

(Fettes, 1999 [Low Quality Evidence]; de Lignieres, 1996 [Low Quality Evidence]; Silberstein, 1993 [Low Quality Evidence])

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## 104. Successful?

Successful is commonly defined as a 50% reduction in frequency in headache days and/or severity of headaches.

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## 105. Consider Changing Delivery System or Formulation of Estrogen and Progestin

Success is achieved through trial and error.

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# On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine Algorithm Annotations

## 109. On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine

Migraine patients who do not have absolute contraindications to estrogen-containing contraceptives should consider that estrogen-containing contraceptives may have unpredictable effects on the severity and/or frequency of headaches. In addition, evidence exists that the risk of ischemic stroke increases for migraineurs using estrogen-containing contraceptives (*International Headache Society Task Force on Combined Oral Contraceptives & Hormone Replacement Therapy, The, 2000 [Guideline]; Becker, 1999 [Low Quality Evidence]; Cupini, 1995 [Low Quality Evidence]*).

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## 111. Evaluate Vascular Risk Factors

### Recommendation:

- Clinicians should evaluate for vascular risk factors before prescribing estrogen containing contraceptives for treatment of migraine.
- Risk factors for coronary artery disease
- Prior thromboembolic disease
- Migraine aura
- Smoking

Women who have migraine with an aura probably have significantly increased ischemic stroke risk if estrogen-containing contraceptives are used. This risk probably increases with age as baseline stroke rates increase, so that the increased risk may be acceptable to the younger patient (i.e., under age 30), but not to the older patient. It is probably too simplistic to say that no patient with migraine with aura should use estrogen-containing contraceptives. The decision should be individualized and should be made with the patient.

It appears reasonable that women who have prolonged migraine auras (certainly those beyond 60 minutes), multiple aura symptoms, or less common aura symptoms (i.e., dysphasia, hemiparesis) should be strongly discouraged from using estrogen-containing contraceptives.

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Patients who develop a migraine aura for the first time while using estrogen-containing contraceptives, or whose previous typical migraine aura becomes more prolonged or complex should discontinue estrogen-containing contraceptives.

Use of oral contraceptives in patients with a history of migraine increases the risk of stroke. [*Conclusion Grade II: See Conclusion Grading Worksheet B – Annotation #111 (Risk of Stroke)*]

Women with migraine aura who smoke and are hypertensive further increase their risk. Additional risk is also noted if they are taking estrogen-containing contraceptives.

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## Migraine Prophylactic Treatment Algorithm Annotations

### 122. Prophylactic Treatment

#### **Recommendation:**

- Clinicians may prescribe prophylactic treatment for patients with migraine history after realistic goals and expectations have been established with the patient.
- **Criteria for prophylactic treatment**
  - Three or more severe migraine attacks per month that fail to respond adequately to symptomatic therapy.
  - Less frequent but protracted attacks that impair the patient's quality of life.
  - Patient is interested in prophylactic treatment.

- **Prophylactic therapy**

Prior to instituting prophylactic therapy for migraine, it is imperative that realistic goals and expectations be established. Patients should have a clear understanding that the goals of preventive therapy are to:

- Decrease migraine attack frequency by 50% or more
- Decrease pain and disability with each individual attack
- Enhance response to acute, specific, anti-migraine therapy

One or more of these goals may be achieved.

- **Medications**

The choice of prophylactic agent depends upon:

- Side-effect profile
- Comorbid conditions
- Medication interactions
- Evidence-based efficacy
- Patient preference (weight loss or gain)

Patients should also understand that there is usually a latency of at least three to six weeks between the initiation of medication and recognizable efficacy. Often, an 8- to 12-week trial is necessary, allowing an adequate period for drug titration to a dosage likely to attain efficacy. It is also not

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uncommon for initial side effects to subside after continued therapy, and patients should be made aware of this so as to avoid premature discontinuation of a potentially effective medication.

The choice of prophylactic medication should be individualized according to the side-effect profile, the presence of comorbid conditions and risk of medication interactions. For example, a tricyclic antidepressant may be especially useful with a migraineur with depression, while sodium valproate may be ideal for a patient with epilepsy.

Reinforce education and lifestyle management. Refer to [Annotation #15, "Evaluate Type of Primary Headache. Initiate Patient Education and Lifestyle Management."](#)

- **Adolescents**

As a prophylactic treatment topiramate, 100 mg/day was effective in reduction of the number of migraine headaches a month (*Lewis, 2009 [High Quality Evidence]*).

**Medications**

The following references pertain to the medications used in prophylactic treatment.

Antiepileptics	Beta-Blockers	Ca++ Channel Blockers	Tricyclics
Valproate sodium ( <i>Hering, 1992 [High Quality Evidence]</i> ; <i>Klapper, 1997 [High Quality Evidence]</i> )	Atenolol ( <i>Johannsson, 1987 [Low Quality Evidence]</i> )	Verapamil ( <i>Solomon, 1983 [High Quality Evidence]</i> )	Amitriptyline ( <i>Couch, 1979 [High Quality Evidence]</i> )
Gabapentin ( <i>Mathew, 2002 [High Quality Evidence]</i> )	Metoprolol		Doxepin
Topiramate ( <i>Brandes, 2004 [High Quality Evidence]</i> ; <i>Silberstein, 2004 [High Quality Evidence]</i> )	Nadolol		Nortriptyline
	Nebivolol ( <i>Schellenberg, 2008 [High Quality Evidence]</i> )		
	Propranolol ( <i>Carroll, 1990 [High Quality Evidence]</i> )		
	Timolol		

**Other Therapies**

The treatment therapies listed below are in alphabetical order and do not indicate work group preference or scientific support.

- **Acupuncture**

A systematic (Cochrane) review of acupuncture in migraine prophylaxis demonstrated that adding acupuncture to patients getting only acute treatment for headaches reduced the number of headaches patients had. When true and sham acupuncture were compared, they both reduced the number of headaches. There was no difference in benefit between true and sham acupuncture groups when results for all trials were pooled. Acupuncture demonstrated slightly better outcomes and fewer adverse effects than drugs shown to be helpful for prophylaxis (*Linde, 2009 [Systematic Review]*).

- **Biofeedback**

Various methods of biofeedback have been used as adjunctive therapy for migraine and tension-type headaches. A meta-analysis of 53 studies of biofeedback in combination with relaxation for

tension-type headache demonstrated these to be more effective than headache monitoring, placebo or relaxation, especially in reducing headache frequency. Most of these studies were randomized controlled trials. Effects were most pronounced in adolescents (*Nestoriuc, 2008 [Meta-analysis]*).

- **Butterbur root (*petasites hybridus*)**

An extract from the plant *Petasites hybridus* is effective for migraine prevention. It should be used to reduce severity and frequency of migraine attacks (*Holland, 2012 [Guideline]*; *Lipton, 2004 [Moderate Quality Evidence]*; *Grossman, 2000 [High Quality Evidence]*).

- **Coenzyme Q10**

In one randomized placebo-controlled trial, coenzyme Q10 was superior to placebo for attack frequency, headache days and days with nausea (*Sándor, 2005 [High Quality Evidence]*).

- **Cognitive behavioral therapy**

This therapy is based on the premise that anxiety and distress aggravate an evolving migraine, and it has the potential for helping the patient recognize maladaptive responses that may trigger a headache (*Campbell, 2003 [Guideline]*; *Andrasik, 1996 [Low Quality Evidence]*; *Reid, 1996 [Low Quality Evidence]*).

Psychological treatments, principally relaxation and cognitive behavioral therapies, are effective treatments of childhood headache (*Eccleston, 2009 [Meta-analysis/Systematic Review]*).

- **Feverfew**

This herbal therapy is made from crushed chrysanthemum leaves. 250 mcg of the active ingredient, parthenolide, is considered necessary for therapeutic effectiveness. Because these are herbal preparations, the quantity of active ingredient varies with the producer (*Vogler, 1998 [Systematic Review]*; *Johnson, 1985 [High Quality Evidence]*).

- **Magnesium**

Daily oral dosages of 400 to 600 mg of this salt have been shown to be of benefit to migraineurs in European studies (*Peikert, 1996 [High Quality Evidence]*).

- **Onabotulinum toxin**

Onabotulinum toxin has been approved by the Food and Drug Administration for the treatment of chronic migraine. Since this approach would be used by headache specialists or others trained specifically for use of this product, onabotulinum toxin is beyond the scope of this discussion.

- **Physical therapy**

Individuals unable to take medication or interested in other nonpharmacological headache management, may benefit from physical therapy including craniocervical exercises. Craniocervical exercises designed to correct postural faults by retraining and strengthening craniocervical flexion, cervicothoracic extension, scapular retraction, thoracic extension and normalization of lumbar lordosis have been shown to significantly reduce tension-type and cervicogenic headaches over a prolonged time frame (*van Ettehoven, 2006 [High Quality Evidence]*; *Jull, 2002 [High Quality Evidence]*).

- **Relaxation training**

Relaxation training includes progressive muscular relaxation, breathing exercises and directed imagery. The goal is to develop long-term skills rather than to treat individual events. Repetitive sessions and practice by the patient increase the success of these therapies in reducing headache frequency (*Reich, 1989 [High Quality Evidence]*).

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- **Riboflavin**

A randomized, placebo-controlled study has found daily supplements of 400 mg moderately effective in reducing the frequency and severity of migraine (*Schoenen, 1998 [High Quality Evidence]*).

**Several additional treatment modalities are available. The modalities listed below lack sufficient scientific support to be recommended as therapies of proven value.**

- **Cervical manipulation**

Previous studies suggested potentially high levels of risk associated with improper application of this modality. Although some studies report few complications, the scientific evidence of significant benefit is not convincing. There is well-documented evidence of cerebral infarction and death from cervical manipulation (*Haldeman, 2002 [Low Quality Evidence]*; *Krueger, 1980 [Low Quality Evidence]*; *Parker, 1980 [High Quality Evidence]*). A systematic review demonstrates that numerous deaths have been associated with high-velocity, short-lever thrusts of the upper spine with rotation (*Ernst, 2010 [Meta-analysis]*).

- **Transcutaneous electrical stimulation units**

Transcutaneous electrical stimulation units for migraine or muscle contraction headache have not been found to be more beneficial than placebo when evaluated in a controlled study (*Solomon, 1985 [High Quality Evidence]*).

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## 124. Continue Treatment for 6-12 Months, Then Reassess

### Recommendation:

- After 6-12 months, a gradual taper of prophylactic migraine treatment is recommended unless headaches become more frequent or more severe.

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## 125. Try Different First-Line Medication or Different Drug of Different Class

### Recommendation:

- Monotherapy is recommended with dose increasing until patient receives benefit, maximum recommended dose is reached or unacceptable side effects occur. If failure with one medication, try another from the same class.

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## 128. Try Combination of Beta-Blockers and Tricyclics

A beta-blocker and tricyclic antidepressant may be more effective and produce fewer side effects in combination than a single drug at a higher dose from either class.

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## 131. Third-Line Prophylaxis Treatment or Consultation with Headache Specialist

Please see [Annotation #42, "Consultation with Headache Specialist."](#)

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The Aims and Measures section is intended to provide protocol users with a menu of measures for multiple purposes that may include the following:

- population health improvement measures,
- quality improvement measures for delivery systems,
- measures from regulatory organizations such as Joint Commission,
- measures that are currently required for public reporting,
- measures that are part of Center for Medicare Services Physician Quality Reporting initiative, and
- other measures from local and national organizations aimed at measuring population health and improvement of care delivery.

This section provides resources, strategies and measurement for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Aims and Measures
- Implementation Recommendations
- Implementation Tools and Resources
- Implementation Tools and Resources Table

## Aims and Measures

1. Increase the accurate diagnosis of primary headaches in patients age 12 years and older. (*Annotation #11*)

Measure for accomplishing this aim:

- a. Percentage of patients diagnosed with primary headache using the appropriate diagnostic criteria.

2. Increase the percentage of patients with primary headache diagnosis who receive educational materials about headache. (*Annotation #15*)

Measure for accomplishing this aim:

- a. Percentage of patients with primary headache who received educational materials on headache.

3. Increase the percentage of patients with primary headache syndrome who receive prophylactic treatment when appropriate. (*Annotations #66, 77, 91, 94, 122, 131*)

Measure for accomplishing this aim:

- a. Percentage of patients with primary headache syndrome who are prescribed prophylactic treatment when appropriate.

4. Increase the percentage of patients with migraine headache who have improvement in their functional status. (*Annotation #15*)

Measures for accomplishing this aim:

- a. Number of days per month with migraine headache.
- b. Percentage of patients with migraine headache who are showing improvement in functional status shown by using one of the following disease-specific tools or questionnaires (e.g., MIDAS, Headache Impact Test (HIT), Migraine Specific Quality of Life [MSQI])\*.
- c. Percentage of patients with migraine headache seen for migraine in the emergency department/urgent care.
- d. Percentage of patients with decreased headache shown by using calendar or diary.

\* While general functional status/quality-of-life assessment tools are easier to administer, disease-specific measures may be easier to interpret for disease-specific disability.

5. Increase the percentage of patients with migraine headache who have a treatment plan or report adherence to a treatment plan for mild, moderate and severe migraine headaches. (*Annotations #32, 33, 36, 42, 43, 44*)

Measures for accomplishing this aim:

- a. Percentage of patients with migraine headache with treatment plans.
- b. Percentage of patients with migraine headache with treatment plan who report adherence to their treatment plan.

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**Aims and Measures**

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6. Decrease the percentage of patients with migraine headache who are prescribed opiates and barbiturates for the treatment of migraines to less than 5%. (*Annotations #36, 49*)

Measure for accomplishing this aim:

- a. Percentage of patients with migraine headache with a prescription for opiates or barbiturates for the treatment of migraine.

7. Increase the percentage of patients with migraine headache who have appropriate acute treatment. (*Annotations #30, 32, 36*)

Measure for accomplishing this aim:

- a. Percentage of patients with migraine headache prescribed appropriate acute treatment.

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## **Aims and Measures**

---

### **Measurement Specifications**

#### **Measure #1a**

Percentage of patients diagnosed with primary headache using the appropriate diagnostic criteria.

#### **Population Definition**

Patients age 12 years and older diagnosed with a primary headache.

#### **Data of Interest**

$$\frac{\# \text{ of patients for which appropriate diagnostic criteria were used}}{\# \text{ of patients diagnosed with a primary headache}}$$

#### **Numerator/Denominator Definitions**

Numerator :        Number of patients age 12 years and older for which appropriate diagnostic criteria were used.

Denominator:      Number of patients age 12 years and older diagnosed with a primary headache.

#### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with one of headache diagnoses: migraine, tension-type, cluster, sinus or chronic daily headache. Determine whether appropriate diagnostic criteria were used to determine diagnosis.

#### **Time Frame Pertaining to Data Collection**

Monthly.

#### **Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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## **Aims and Measures**

---

### **Measure #2a**

Percentage of patients with a primary headache who received educational materials on headache.

### **Population Definition**

Patients age 12 years and older with a primary headache.

### **Data of Interest**

$$\frac{\text{\# of patients who received educational materials on headache}}{\text{\# of patients with a primary headache}}$$

### **Numerator/Denominator Definitions**

Numerator : Number of patients age 12 years and older with primary headache, who received educational materials on headache. This can include information about:

- Genetic predisposition to migraine
- Role of lifestyle changes
- Stress reduction, regular eating and sleeping schedules, and regular aerobic exercise
- Results of overuse of analgesics and acute migraine drugs
- Benefit of keeping a headache diary
- Treatment approaches

Denominator: Number of patients age 12 years and older with a primary headache.

### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with a primary headache. Review records to determine whether patients received written educational materials on headache.

### **Time Frame Pertaining to Data Collection**

Monthly.

### **Notes**

Providing education is of paramount importance in managing any chronic illness; it is especially important in the ongoing management of migraine. Patients may have to make lifestyle changes and are often required to make self-management choices in the treatment of individual headaches and to maintain a diary to clarify the frequency, severity, triggers and treatment responses to their headaches.

This is a process measure, and improvement is noted as an increase in the rate.

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## **Aims and Measures**

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### **Measure #3a**

Percentage of patients with primary headache syndrome who are prescribed prophylactic treatment when appropriate.

### **Population Definition**

Patients age 12 years and older with primary headache syndrome.

### **Data of Interest**

$$\frac{\text{\# of patients who are prescribed prophylactic treatment when appropriate}}{\text{\# of patients with headache diagnosis}}$$

### **Numerator/Denominator Definitions**

Numerator :      Number of patients age 12 years and older with primary headache syndrome who are prescribed prophylactic treatment when appropriate.

Denominator:      Number of patients age 12 years and older with primary headache diagnosis syndrome.

### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with primary headache syndrome.  
Review records to determine whether patients were prescribed prophylactic treatment when appropriate.

### **Time Frame Pertaining to Data Collection**

Monthly.

### **Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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## **Aims and Measures**

---

### **Measure #4a**

Number of days per month with migraine headache.

### **Population Definition**

Patients age 12 years and older with diagnosis of migraine headache.

### **Data of Interest**

Number of days per month with migraine for patients who are diagnosed with migraine headache.

### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with diagnosis of migraine headache.  
Review records to determine the number of days per month the patients had migraine.

### **Time Frame Pertaining to Data Collection**

Monthly.

### **Notes**

This is an outcome measure, and the goal is a decrease in days with migraine.

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## **Aims and Measures**

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### **Measure #4b**

Percentage of patients with migraine headache who are showing improvement in functional status shown by using one of the following disease-specific tools or questionnaires (e.g., MIDAS, Headache Impact Test (HIT), Migraine Specific Quality of Life [MSQ])\*.

\* While general functional status/quality of life assessment tools are easier to administer, disease-specific measures may be easier to interpret for disease-specific disability. Tools can be found at <http://www.headaches.org>.

### **Population Definition**

Patients age 12 years and older with diagnosis of migraine headache.

### **Data of Interest**

$$\frac{\text{\# of patients who are assessed for functional status using disease-specific tools}}{\text{\# of patients with migraine headache diagnosis}}$$

### **Numerator/Denominator Definitions**

Numerator : Number of patients age 12 years and older and migraine headache diagnosis, who are showing improvement in functional status shown by using one of the following disease-specific tools or questionnaires (e.g., MIDAS, Headache Impact Test, Migraine Specific Quality of Life).

Denominator: Number of patients age 12 years and older with migraine headache diagnosis.

### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with migraine headache diagnosis. Review records to determine whether patients were assessed for functional status using disease-specific tools or questionnaires such as MIDAS, HIT or MSQ.

### **Time Frame Pertaining to Data Collection**

Monthly.

### **Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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**Aims and Measures**

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**Measure #4c**

Percentage of patients with migraine headache seen for migraine in the emergency department/urgent care.

**Population Definition**

Patients age 12 years and older with diagnosis of migraine headache.

**Data of Interest**

$$\frac{\# \text{ of patients seen for migraine in the emergency department/urgent care}}{\# \text{ of patients with migraine headache diagnosis}}$$

**Numerator/Denominator Definitions**

Numerator :        Number of patients age 12 years and older and migraine headache diagnosis who are seen for migraine in the emergency department/urgent care.

Denominator:      Number of patients age 12 years and older with migraine headache diagnosis.

**Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with migraine headache diagnosis. Review records to determine whether patients were seen for migraine in the emergency department/urgent care.

**Time Frame Pertaining to Data Collection**

Monthly.

**Notes**

This is an outcome measure, and improvement is noted as a decrease in the rate.

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**Aims and Measures**

---

**Measure #4d**

Percentage of patients with decreased migraine headache shown by using a calendar or diary.

**Population Definition**

Patients age 12 years and older with diagnosis of migraine headache.

**Data of Interest**

$$\frac{\text{\# of patients who have a headache calendar or diary}}{\text{\# of patients with migraine headache diagnosis}}$$

**Numerator/Denominator Definitions**

Numerator :        Number of patients age 12 years and older and migraine headache diagnosis, who have headache calendar or diary.

Denominator:      Number of patients age 12 years and older with migraine headache diagnosis.

**Method/Source of Data Collection**

Review electronic medical records for atients age 12 years and older with migraine headache diagnosis.  
Review records to determine whether patients reported having headache calendar or diary.

**Time Frame Pertaining to Data Collection**

Monthly.

**Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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**Aims and Measures**

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**Measure #5a**

Percentage of patients with migraine headache with treatment plans.

**Population Definition**

Patients ages 12 years and older with diagnosis of migraine headache.

**Data of Interest**

$$\frac{\text{\# of patients who have a treatment plan}}{\text{\# of patients with migraine headache diagnosis}}$$

**Numerator/Denominator Definitions**

Numerator :       Number of patients age 12 years and older and migraine headache diagnosis, who have a treatment plan.

Denominator:     Number of patients age 12 years and older with a migraine headache diagnosis.

**Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with migraine headache diagnosis.  
Review records to determine whether patients had treatment plan.

**Time Frame Pertaining to Data Collection**

Monthly.

**Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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## **Aims and Measures**

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### **Measure #5b**

Percentage of patients with migraine headache with a treatment plan who report adherence to their treatment plan.

### **Population Definition**

Patients age 12 years and older with diagnosis of migraine headache and have a treatment plan.

### **Data of Interest**

$$\frac{\text{\# of patients who report adherence to their treatment plan}}{\text{\# of patients with migraine headache diagnosis and treatment plan}}$$

### **Numerator/Denominator Definitions**

Numerator : Number of patients age 12 years and older and migraine headache diagnosis and treatment plan who report adherence to their treatment plan.

Denominator: Number of patients age 12 years and older with migraine headache diagnosis and treatment plan.

### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with migraine headache diagnosis and treatment plan. Review records to determine whether patients report adherence to their treatment plan.

### **Time Frame Pertaining to Data Collection**

Monthly.

### **Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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## **Aims and Measures**

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### **Measure #6a**

Percentage of patients with migraine headache with a prescription for opiates or barbiturates for the treatment of migraine.

### **Population Definition**

Patients age 12 years and older with diagnosis of migraine headache.

### **Data of Interest**

$$\frac{\text{\# of patients prescribed opiates or barbiturates for the treatment of migraine}}{\text{\# of patients with migraine headache diagnosis}}$$

### **Numerator/Denominator Definitions**

Numerator : Number of patients age 12 years and older and migraine headache diagnosis who are prescribed opiates or barbiturates for the treatment of migraine.

Denominator: Number of patients age 12 years and older with migraine headache diagnosis.

### **Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with migraine headache diagnosis. Review records to determine whether patients were prescribed opiates or barbiturates for the treatment of migraine.

### **Time Frame Pertaining to Data Collection**

Monthly.

### **Notes**

This is a process measure, and improvement is noted as a decrease in the rate to less than 5% usage in a facility. This measure is intended to address overuse in prescription on opioids and narcotics for the treatment of migraine headache.

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**Aims and Measures**

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**Measure #7a**

Percentage of patients with migraine headache prescribed appropriate acute treatment.

**Population Definition**

Patients age 12 years and older with diagnosis of migraine headache.

**Data of Interest**

$$\frac{\text{\# of patients prescribed appropriate acute treatment}}{\text{\# of patients with migraine headache diagnosis}}$$

**Numerator/Denominator Definitions**

Numerator :        Number of patients age 12 years and older and migraine headache diagnosis who are prescribed appropriate acute treatment.

Denominator:      Number of patients age 12 years and older with migraine headache diagnosis.

**Method/Source of Data Collection**

Review electronic medical records for patients age 12 years and older with migraine headache diagnosis.  
Review records to determine whether patients were prescribed appropriate acute treatment.

**Time Frame Pertaining to Data Collection**

Monthly.

**Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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## Implementation Recommendations

Prior to implementation, it is important to consider current organizational infrastructure that address the following:

- System and process design
- Training and education
- Culture and the need to shift values, beliefs and behaviors of the organization.

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline:

- Develop a system for assessment of headache based on history and functional impairment.
- Develop a system for results of this assessment to be used for identification of treatment options/recommendations.
- Develop systems that allow for consistent documentation and monitoring based on type of headache.
- Develop a system for follow-up assessment that identifies success in management of headache in the primary care setting.
- Develop a process that will remove barriers to referral to a specialist if indicated.
- Develop a system for consistent documentation and monitoring of medication administration.

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## Implementation Tools and Resources

### Criteria for Selecting Resources

The following tools and resources specific to the topic of the guideline were selected by the work group. Each item was reviewed thoroughly by at least one work group member. It is expected that users of these tools will establish the proper copyright prior to their use. The types of criteria the work group used are:

- The content supports the clinical and the implementation recommendations.
- Where possible, the content is supported by evidence-based research.
- The author, source and revision dates for the content are included where possible.
- The content is clear about potential biases and when appropriate conflicts of interests and/or disclaimers are noted where appropriate.

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## Implementation Tools and Resources Table

Author/Organization	Title/Description	Audience	Web Sites/Order Information
American Academy of Family Physicians	General health information on various topics.	Patients and Families	<a href="http://familydoctor.org/family-doctor/en.html">http://familydoctor.org/family-doctor/en.html</a>
American Headache Society® (AHS) Committee for Headache Education	This Web site is an excellent resource for patients and clinicians to learn more about headaches and resources to help manage them, including prevention and treatment. This site also has information on migraine assessments and headache diaries.	Health Care Professionals; Patients and Families	<a href="http://www.americanheadachesociety.org">http://www.americanheadachesociety.org</a>
Headache Care	This Web site is designed for viewers to educate themselves on types of headaches, treatment and prevention techniques. This site contains a complete migraineur's guide to migraine that will help patients understand migraines and how they can become an active participant in their care program to gain control over migraines.	Patients and Families	<a href="http://www.headachecare.com">http://www.headachecare.com</a>
Healthfinder	General health information on various topics. Spanish link available.	Patients and Families	<a href="http://www.healthfinder.gov">http://www.healthfinder.gov</a>
HealthPartners Medical Group	General overview on various topics and health information. (Need to register prior to accessing information.)	Patients and Families	<a href="http://www.healthpartners.com">http://www.healthpartners.com</a>
ICSI	ICSI Shared Decision-Making Model	Providers	<a href="http://www.icsi.org">http://www.icsi.org</a>
Mayo Clinic	General health information on various topics and interactive "Ask a Specialist" and Headache Center: A Complete Guide to Managing Headaches.	Patients and Families	<a href="http://www.mayoclinic.com">http://www.mayoclinic.com</a>
National Library of Medicine's MEDLINE plus National Institutes of Health	MedlinePlus is the National Institutes of Health's Web site for patients and their families and friends. Produced by the National Library of Medicine, it provides information about diseases, conditions and wellness issues.	Health Care Professionals; Patients and Families	<a href="http://www.nlm.nih.gov/medlineplus">http://www.nlm.nih.gov/medlineplus</a>
National Women's Health Information Center	Government resource for women's health information and referrals. Spanish language link.	Patients and Families	<a href="http://www.4woman.org">http://www.4woman.org</a>
National Headache Foundation	Educational and informational resources on headache.	Patients and Families; Health Care Professionals	<a href="http://headaches.org">http://headaches.org</a>

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**Implementation Tools and Resources Table**

<b>Author/Organization</b>	<b>Title/Description</b>	<b>Audience</b>	<b>Web Sites/Order Information</b>
Primary Care Network	Patient-centered strategies for effective management of migraine headaches.	Health Care Professionals	<a href="http://www.primarycarenet.org">http://www.primarycarenet.org</a>
Quality Metric Incorporated	General health assessment tools including the Headache Impact Test (HIT). (Need to register prior to accessing information.)	Health Care Professionals; Patients and Families	<a href="http://www.amihealthy.com">http://www.amihealthy.com</a>

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The subdivisions of this section are:

- Conclusion Grading Worksheet Summary
  - Conclusion Grading Worksheets
- References
- Appendices

## Conclusion Grading Worksheet Summary

**Grade I:** The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

**Grade II:** The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

**Grade III:** The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

**Grade Not Assignable:** There is no evidence available that directly supports or refutes the conclusion.

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# Conclusion Grading Worksheet A – Annotation #91 (Non-Steroidal Anti-Inflammatory Drugs)

**Work Group's Conclusion:** Non-steroidal anti-inflammatory drugs should be considered approaches of first choice in the prophylactic treatment of migraine associated with menses. Many clinicians consider triptans to be equally effective, but there are no comparative studies.

**Conclusion Grade: III**

Author/Year	Design Type	Quality	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ <i>Work Group's Comments (italicized)</i>																								
Sargent, Solbach, Damasia, et al. (1985)	RCT	High	-Ages 18 to 65 years with confirmed diagnosis of common or classical migraine, or combination of migraine and muscle contraction headache (history of migraines for ≥1 yr, average of 12 migraine headache days over ≥6 migraine attacks in 3 months prior to entry) -Excluded: pregnant, major medical illness, active ulcers in previous year, bleeding problems, sensitivity to NSAIDs, rebound ergotamine migraine, contraindications to propranolol hydrochloride -Randomized to naproxen sodium (NS) (550 mg bid), propranolol hydrochloride (PH) (40 mg tid) or placebo (PL) -Patients could not take other NSAIDs, anticoagulants, or alpha-adrenergic antagonists during study period	-129 patients were included in the efficacy analysis (42 in NS group, 44 in PH group, and 43 in PL group); groups were comparable (demographic and clinical data) at baseline -Median outcomes (Patient daily improvement record): <table border="1" style="margin-left: 20px;"> <tr> <td></td> <td>NS</td> <td>PH</td> <td>PL</td> </tr> <tr> <td>Headache days per week</td> <td>-0.05</td> <td>0.33</td> <td>-0.25*</td> </tr> <tr> <td>Headache severity</td> <td>0.83</td> <td>1.00</td> <td>0.66*</td> </tr> <tr> <td>Nausea</td> <td>1.42</td> <td>1.66</td> <td>1.37*</td> </tr> <tr> <td>Vomiting</td> <td>1.88</td> <td>1.92</td> <td>1.72*</td> </tr> <tr> <td>Visual disturbances</td> <td>1.80</td> <td>1.30</td> <td>1.18*</td> </tr> </table> *No significant differences among groups -Data from 30 patients who reported at least 2 menstrual periods during the study period: frequency of migraine before start of menses was lower than after start of menses in both treatment groups (comparisons with placebo group were not significant, however); NS reduced severity of migraine before start of menses (relative to after start of menses) more than placebo (p=0.01) or PH (p=0.054) -More gastrointestinal complaints in NS group than PH group (p=0.02)		NS	PH	PL	Headache days per week	-0.05	0.33	-0.25*	Headache severity	0.83	1.00	0.66*	Nausea	1.42	1.66	1.37*	Vomiting	1.88	1.92	1.72*	Visual disturbances	1.80	1.30	1.18*	-NS and PH appeared to reduce headache frequency, headache severity, nausea and visual disturbances relative to placebo although the differences were not significant. PH was better tolerated than NS. Women treated with NS experienced the greatest decrease in headache severity during the pre-menstrual period.  NOTES: 12-week full-dose phase (III) (all received PL) followed a 2-week washout phase (I) and 2 weeks where PH group received 40 mg bid (II) (NS group received full dose); 170 were enrolled, 161 entered washout (I), 149 entered phase II, and 129 completed phase III (efficacy data phase); excluded 20 who had entered phase III from analysis (14 with fewer than 4 wks of treatment, 6 with protocol violations)  <i>Work Group's Comments: no explanation given for why 170 were enrolled but 149 entered active treatment phase; compliance with medication was not reported; little detail about measurement tools used</i>
	NS	PH	PL																										
Headache days per week	-0.05	0.33	-0.25*																										
Headache severity	0.83	1.00	0.66*																										
Nausea	1.42	1.66	1.37*																										
Vomiting	1.88	1.92	1.72*																										
Visual disturbances	1.80	1.30	1.18*																										

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Author/Year	Design Type	Quality	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ <i>Work Group's Comments (italicized)</i>
Sances, Martignoni, Fioroni, et al. (1990)	Non Random	Low	-Ages 19 to 45 years; migraine without aura; menstrual-related periodicity of migraine for 2 to 30 years (headaches every cycle); free from endocrinological, metabolic or other organic abnormalities; no prophylactic treatment for migraine or no oral contraceptives for 6 months prior to study -2-month observation period -3-month (3 cycles) double-blind treatment with naproxen sodium (NS) or placebo (PL); treatment from 7 <sup>th</sup> day before expected menses through 6 <sup>th</sup> day of flow -3 additional cycles with all women treated with active drug -Calculated Pain Total Index (PTI) from daily diaries based on number of attacks, duration and severity	-35 completed the study (of 40 enrolled); 18 with NS for 6 mos, 17 with PL for 3 mos and NS for 3 months; 2 groups comparable (age, history of disease, and migraine attack features); estradiol, progesterone and prolactin levels normal for all patients in each cycle in which they were tested -Percentage of response to treatment did not significantly differ between NS and PL groups in double-blind phase; response was almost equal in open phase; absence of migraine reported in 16.7% of NS group in 1 <sup>st</sup> month of treatment and 33% in 2 <sup>nd</sup> and 3 <sup>rd</sup> months (compared to none in PL group) -NS group had significant change in PTI (relative to baseline) throughout study period (p=0.05 at month 2, others p<0.01); PL group had significant change in PTI at 1 <sup>st</sup> month (p<0.05) and at months 3-6 (all p<0.01); overall no difference between NS and PL -Days of headache: decreased throughout study period for NS group (all p<0.005) and at months 1, 2, 4, 5 & 6 for PL group (p=0.05 at month 2, others p<0.005); NS group differed from PL group at month 3 (p<0.05) -Analgesic consumption: decreased throughout study period for NS group (all p<0.01) and at months 1, 4, 5 & 6 for PL group (all p<0.01); NS group significantly different from PL group at months 1 (p<0.02), 2 and 3 (both p<0.05) -Menstrual Distress Questionnaire: significant improvement (p<0.006) in premenstrual and menstrual pain during NS treatment but not PL treatment	-In comparison with placebo, NS is effective in reducing headache intensity and duration as well as days of headache and analgesic consumption. Good tolerability and few side effects were observed.  NOTES: 3 dropped out for reasons unrelated to treatment; 2 dropped out due to severe gastralgia and nausea; non-significant differences in PTI between NS and PL were attributed to high variability of scores and high standard deviations

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# Conclusion Grading Worksheet B – Annotation #111 (Risk of Stroke)

**Work Group's Conclusion:** Use of oral contraceptives in patients with a history of migraine increases the risk of stroke.

## Conclusion Grade: II

Author/Year	Design Type	Quality	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ <i>Work Group's Comments (italicized)</i>																																				
Tzourio, Tehindrazanarivo, Iglésias, et al. (1995)	Case-Control	Low	<p>-Cases: 72 women under age 45 years hospitalized for first ischemic stroke</p> <p>-Controls: 173 women who agreed to participate from among 225 randomly selected patients hospitalized in same centers during same time for acute orthopedic or benign rheumatological illness</p> <p>-Interviewed (telephone) cases and controls about history of headaches and vascular risk factors; subjects were not aware of aim of study</p>	<p>-Baseline characteristics: no differences in age, BMI, history of diabetes, educational background, or hormonal content of oral contraceptives; smoking status, oral contraceptive use status, and history of hypercholesterolemia differed between groups</p> <p>-No association between migraine and present use of oral contraceptives in cases or controls</p> <p>-Migraine and ischemic stroke were strongly associated (60% of cases vs. 30% of controls; p&lt;0.001); association persisted after controlling for age, history of hypertension, use of oral contraceptives, and smoking</p> <p>-In migrainous women using oral contraceptives (at time of stroke for cases, at time of interview for controls), risk of stroke was 13.9 (OR=13.9; 95%CI: 5.5-35.1) compared to those without migraine not using oral contraceptive</p>	<p>-Migraine is strongly associated with ischemic stroke in young women independent of main vascular risk factors. The risk of ischemic stroke was particularly increased for migrainous women who were currently using oral contraceptives.</p> <p>NOTE: used a group of 57 women under age 45 hospitalized for orthopedic conditions to determine expected prevalence of migraine in controls (since non-response in controls might be an issue); 73% of the stroke patients and 74% of the controls using oral contraceptives were taking 30-40 µg (micrograms) of estrogen.</p> <p><i>Work Group's Comments: investigators used a structured interview to reduce potential for classification bias; recall bias is possible</i></p>																																				
Becker (1999)	Review	Low		<p>-Assumptions:</p> <ol style="list-style-type: none"> <li>Women with migraine with aura have relative stroke risk of approximately 6</li> <li>Low-dose oral contraceptives with estrogen content below 50 µg have increased ischemic stroke risk of approximately 2</li> <li>If a patient with migraine with aura uses oral contraceptives and if the odds ratios are multiplicative, the expected relative ischemic stroke risk might be 6*2=12</li> </ol> <p>-Expected incidence of ischemic stroke per 100,000 women per year:</p> <table border="1"> <thead> <tr> <th>Age</th> <th>Without Migraine</th> <th>Migraine with No OC use</th> <th>OC use</th> </tr> </thead> <tbody> <tr> <td>Aura</td> <td></td> <td></td> <td></td> </tr> <tr> <td>15-19</td> <td>0.4</td> <td>0.8</td> <td>2</td> </tr> <tr> <td>20-24</td> <td>1.4</td> <td>3</td> <td>8</td> </tr> <tr> <td>25-29</td> <td>1.9</td> <td>4</td> <td>11</td> </tr> <tr> <td>30-34</td> <td>2.4</td> <td>5</td> <td>14</td> </tr> <tr> <td>35-39</td> <td>3.4</td> <td>7</td> <td>20</td> </tr> <tr> <td>40-44</td> <td>11.6</td> <td>23</td> <td>70</td> </tr> <tr> <td></td> <td></td> <td></td> <td>139</td> </tr> </tbody> </table>	Age	Without Migraine	Migraine with No OC use	OC use	Aura				15-19	0.4	0.8	2	20-24	1.4	3	8	25-29	1.9	4	11	30-34	2.4	5	14	35-39	3.4	7	20	40-44	11.6	23	70				139	<p>-Risk for ischemic stroke associated with migraine without aura is probably low enough that it is not a major consideration in prescribing oral contraceptives unless the patient has other major risk factors or unless headaches become substantially exacerbated</p> <p>-For patients with migraine with aura or who develop migraine while taking oral contraceptives, the additional ischemic stroke risk should be considered in clinical practice</p>
Age	Without Migraine	Migraine with No OC use	OC use																																						
Aura																																									
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Links are provided for those new references added to this edition (author name is highlighted in blue).

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## **Appendix A – Drug Treatment for Headache**

Note: As there are multiple, easy-to-access information sources available that contain current detailed drug information, the tables on the following pages highlight only those selected drugs, their dosing, side effect and contraindications that may be otherwise challenging to locate. Therefore, this is not intended as an inclusive listing of medication treatment options. All drugs are listed in alphabetical order, not in order of work group preference. Drugs are listed by their generic names and include brand names only where the generic name may not be well recognized. These drug treatment tables have been compiled from package inserts, PDR.net and Micromedex.

When viewing the following Drug Treatment tables, please consider the following key for the symbols used in each table:

- \* Patient, lying down supine, head extended 45 degrees and rotated 30 degrees, drips 0.4 mL of 4% lidocaine solution in the nostril ipsilateral to headache when unilateral, or most clear nostril when headache is bilateral.
- \*\* Please note use of parenteral corticosteroids should be considered as treatment of last resort and initiated only after careful consideration of the risks as they pertain to each individual. Their use is empiric and based upon anecdotal evidence. The rationale for the use of corticosteroids is uncertain, but they may reduce perivascular inflammation or sensitize the blood vessels to the vasoconstrictive effect of circulating catecholamines and specific anti-migraine agents.
- \*\*\* Ergotamine is not commonly used and not recommended as a first-line treatment.

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**Appendix A – Drug Treatment for Headache**

The following references pertain to medications used in migraine treatment.

<b>Almotriptan:</b> (Spierings, 2001 [High Quality Evidence])	<b>Magnesium Sulfate:</b> (Demirkaya, 2001 [Low Quality Evidence])
<b>Acetaminophen, aspirin, caffeine combination:</b> Because there is no good evidence to support the use of acetaminophen for treatment of mild migraine, the work group has replaced it with acetaminophen, aspirin and caffeine (Lipton, 1998 [High Quality Evidence]; Stang, 1994 [Low Quality Evidence]).	<b>Meperidine:</b> (Duarte, 1992 [High Quality Evidence])
<b>Chlorpromazine – IM:</b> (McEwen, 1987 [High Quality Evidence])	<b>Metoprolol:</b> (Gerber, 1991 [High Quality Evidence]; Sørensen, 1991 [High Quality Evidence])
<b>Chlorpromazine – IV:</b> (Lane, 1989 [High Quality Evidence])	<b>Nadolol:</b> (Ryan, 1983 [High Quality Evidence]; Ryan, 1982 [High Quality Evidence])
<b>Dexamethasone – IM:</b> (Gallagher, 1986 [Low Quality Evidence])	<b>Naproxen:</b> (Krymchantowski, 2000 [Low Quality Evidence]; Nestvold, 1985 [High Quality Evidence])
<b>Dichloralphenazone:</b> (Diamond, 1976 [High Quality Evidence])	<b>Naratriptan:</b> (Mathew, 1997 [High Quality Evidence])
<b>Dihydroergotamine:</b> (Callahan, 1986 [High Quality Evidence])	<b>Nortriptyline:</b> (Adelman, 1995 [Low Quality Evidence])
<b>Dihydroergotamine – nasal:</b> (Gallagher, 1996 [High Quality Evidence])	<b>Prochlorperazine – IV:</b> (Coppola, 1995 [High Quality Evidence])
<b>Dihydroergotamine- IM:</b> (Weisz, 1994 [Low Quality Evidence])	<b>Prochlorperazine – rectal:</b> (Jones, 1994 [High Quality Evidence])
<b>Dihydroergotamine- SQ:</b> (Winner, 1996 [High Quality Evidence])	<b>Promethazine:</b> (Capobianco, 1996 [Guideline])
<b>Doxepin:</b> (Adelman, 1995 [High Quality Evidence])	<b>Rizatriptan:</b> (Kramer, 1998 [High Quality Evidence]; Teall, 1998 [High Quality Evidence])
<b>Eletriptan:</b> (Stark, 2002 [High Quality Evidence])	<b>Sumatriptan – nasal:</b> (Francis, 2010 [Moderate Quality Evidence]; Ryan, 1997 [High Quality Evidence])
<b>Hydroxyzine:</b> (Duarte, 1992 [High Quality Evidence])	<b>Sumatriptan – oral:</b> (Cutler, 1995 [High Quality Evidence]; Sargent, 1995 [High Quality Evidence])
<b>Ibuprofen:</b> (Kloster, 1992 [High Quality Evidence])	<b>Sumatriptan – SQ:</b> (Wendt, 2006 [High Quality Evidence]; Visser, 1992 [High Quality Evidence]; Subcutaneous Sumatriptan International Study Group, 1991 [High Quality Evidence])
<b>Isometheptene:</b> (Diamond, 1976 [High Quality Evidence])	<b>Sumatriptan/Naproxen:</b> (Brandes, 2007 [High Quality Evidence])
<b>Ketorolac:</b> (Duarte, 1992 [High Quality Evidence])	<b>Valproate Sodium:</b> (Mathew, 2000 [Low Quality Evidence]; Norton, 2000 [Low Quality Evidence])
<b>Lidocaine – nasal:</b> (Maizels, 1996 [High Quality Evidence])	<b>Zolmitriptan:</b> (Charlesworth, 2003 [High Quality Evidence]; Dowson, 2003 [High Quality Evidence]; Rapoport, 1997 [High Quality Evidence]; Solomon, 1997 [High Quality Evidence])

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Appendix A – Drug Treatment for Headache

Drug	Dose	Side Effects	Contraindications
<b>Chlorpromazine (CPZ) Injection</b>	<ul style="list-style-type: none"> <li>Dilute 1 mL CPZ (25 mg) with 4 mL normal saline (1 mL = 5 mg CPZ)</li> <li>0.1 mg/kg IV every 15 minutes, up to 3 doses. Dilute to 1 mg/mL with normal saline and administer via IV infusion at rate to greater than 1 mg/min.</li> <li>Stop when headache relieved; not to exceed 25 mg/dose</li> </ul>	Drowsiness, extrapyramidal symptoms	Hypotension, previous adverse reaction
<b>Dexamethasone Injection**</b>	4-20 mg IM once per month	Cushingoid	
<b>DHE (dihydroergotamine mesylate) Injection</b>	0.5-1 mg subcutaneous, IM or IV, may repeat in 1 hour; not to exceed 3 mg in 24 hours IM or 2 mg IV	Nausea, vomiting, diarrhea, abdominal cramps, dizziness, paresthesia and leg pain	Pregnancy, history of ischemic heart disease, history of Prinzmetal's angina, severe peripheral vascular disease, onset of chest pain following administration of test dose, within 24 hours of receiving any triptan or ergot derivative, elevated blood pressure, patients with hemiplegic or basilar-type migraines†, cerebrovascular disease
<b>Nasal spray</b>	0.5 mg in each nostril; repeat 0.5 mg in each nostril in 15 min; not to exceed 6 sprays (3 mg) in 24 hours	Nasal congestion, throat discomfort, nasal irritation, nausea, chest tightness, tingling, vomiting	See DHE injection
<b>Hydrocortisone Injection**</b>	<ul style="list-style-type: none"> <li>100-250 mg IM</li> <li>Repeat parenteral or oral equivalent may be given within 24 hrs</li> </ul>		
<b>Isometheptene Mucate 65 mg Dichloralphenazone 100 mg Acetaminophen 325 mg Midrin® CIV</b>	2 by mouth at onset; 1 every hr as needed; not to exceed 5 in 12 hrs; not to exceed 2 treatment days per week or 40 caps per month	Drowsiness, dizziness	Ischemic heart disease, severe renal disease, ischemic cerebrovascular disease
<b>Lidocaine 4% Solution*</b>	0.4 ml-0.5 mL intranasally over 30 seconds	Burning or numbness in nose or pharynx	

Refer to the first page of Appendix A for the key explaining the symbols.

Many of the medications listed are available in a variety of formulations for different routes of administration (e.g., oral, intravenous, rectal suppository).

† Basilar-type migraine is defined as three of the following features: diplopia, diparthria, tinnitus, vertigo, transient hearing loss or mental confusion (*Headache Classification Subcommittee of the International Headache Society, 2004 [Guideline]*)

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**Appendix A – Drug Treatment for Headache**

<b>Drug</b>	<b>Dose</b>	<b>Side Effects</b>	<b>Contraindications</b>
<b>Magnesium Sulfate Injection</b>	1 gm IV	Flushing, hypotension, burning sensation in the face and neck	Heart block, severe renal impairment
<b>Prochlorperazine IV</b>	<ul style="list-style-type: none"> <li>• Dilute 1 mL (10 mg) with 4 mL normal saline (1 mL = 2 mg)</li> <li>• Inject 1 mL /3-5 min; stop when headache relieved; not to exceed 10 mg/dose</li> </ul>	Drowsiness, extrapyramidal symptoms	Hypotension
<b>Valproate Sodium Injection</b>	300-500 mg IV in normal saline at a rate of 20 mg/minute	Nausea, vomiting, tremor, dizziness	Liver disease, pregnancy

Refer to the first page of Appendix A for the key explaining the symbols.

Many of the medications listed are available in a variety of formulations for different routes of administration (e.g., oral, intravenous, rectal suppository).

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## Appendix B – Drug Treatment for Adjunctive Therapy

<b>Drug</b>	<b>Dose</b>	<b>Side Effects</b>
<b>Caffeine</b>	Minimum 65 mg by mouth	Tremors, nausea
<b>Metoclopramide</b>	10 mg IV	Drowsiness, extrapyramidal symptoms
<b>Prochlorperazine</b>	5-10 mg IV, IM, or rectal suppository 25 mg	Drowsiness, extrapyramidal symptoms
<b>Promethazine</b>	25 mg IV over 1 minute, IM, or rectal suppository	Drowsiness, extrapyramidal symptoms

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## Appendix C – Headache Clinical Summary

Diagnosis of Headache Type*	
<ul style="list-style-type: none"> <li>• Accurate diagnosis of primary headache requires a thorough physical exam and detailed headache history to rule out secondary causes (e.g., hematoma, tumor, metabolic disorders, craniocervical arterial dissection, hydrocephalus, etc.).</li> <li>• Neuroimaging, EEG, lumbar puncture, or cerebrospinal fluid and blood studies may be indicated to evaluate for secondary causes. These tests are <b>not</b> indicated for primary headache diagnosis.</li> <li>• <b>Warning signs of possible disorder other than primary headache:</b> <ul style="list-style-type: none"> <li>○ Headaches that worsen over weeks or months</li> <li>○ New or different headache or "worst headache ever"</li> <li>○ Sudden, severe onset or "thunderclap" headache</li> <li>○ New onset of headaches after age 50</li> <li>○ Seizures</li> <li>○ Symptoms suggestive of systemic disorder: fever, hypertension, myalgia, scalp tenderness, or weight loss</li> <li>○ Persistent headache brought on by cough, sneeze, bending over, or physical or sexual exertion</li> <li>○ Neurological signs suggestive of secondary cause: confusion, altered level of consciousness, memory impairment, papilledema, visual field defect, cranial nerve asymmetry, extremity weaknesses, clear sensory deficits, reflex asymmetry, extensor plantar response, or gait disturbances</li> </ul> </li> </ul>	
Criteria for Primary Headache Types	
<ul style="list-style-type: none"> <li>• <b>Migraine with or without aura**:</b> <ul style="list-style-type: none"> <li>○ Two or more of the following:                             <ul style="list-style-type: none"> <li>▪ Unilateral location</li> <li>▪ Pulsating or throbbing quality</li> <li>▪ Moderate to severe intensity</li> <li>▪ Aggravated by routine activity</li> </ul> </li> <li>○ Plus 1 or both of the following:                             <ul style="list-style-type: none"> <li>▪ Nausea/vomiting</li> <li>▪ Photophobia and phonophobia</li> </ul> </li> <li>○ Previous similar headaches</li> <li>○ <b>Aura criteria:</b> <ul style="list-style-type: none"> <li>▪ One or more reversible aura symptoms</li> <li>▪ One or more aura symptoms develop over more than 4 minutes, or two or more symptoms occur in succession</li> <li>▪ Symptoms do not last more than 60 minutes</li> <li>▪ Headache follows within 60 minutes</li> </ul> </li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Cluster headache**:</b> <ul style="list-style-type: none"> <li>○ Frequency: one every other day to 8 per day</li> <li>○ Severe unilateral orbital, supraorbital and/or temporal pain</li> <li>○ Pain lasting 15 to 180 minutes untreated</li> <li>○ One or more of the following occur on same side as the pain:                             <ul style="list-style-type: none"> <li>▪ Conjunctival injection</li> <li>▪ Lacrimation (tearing)</li> <li>▪ Nasal congestion</li> <li>▪ Rhinorrhea</li> <li>▪ Forehead and facial swelling</li> <li>▪ Miosis (constricted pupil)</li> <li>▪ Ptosis (eyelid drooping)</li> <li>▪ Eyelid edema</li> <li>▪ Agitation, unable to lie down</li> </ul> </li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>• <b>Tension-type headache (Chronic and Episodic)**:</b> <ul style="list-style-type: none"> <li>○ Two or more of the following:                             <ul style="list-style-type: none"> <li>▪ Bilateral location</li> <li>▪ Pressing or tightening quality</li> <li>▪ Mild to moderate intensity</li> <li>▪ Not aggravated by routine activity</li> </ul> </li> <li>○ For <b>Chronic</b>, all of the following:                             <ul style="list-style-type: none"> <li>▪ Frequency: average of 15 or more headache days per month for more than 3 months</li> <li>▪ No vomiting</li> <li>▪ No more than one of nausea, photophobia, or phonophobia</li> </ul> </li> <li>○ For <b>Episodic</b>, all of the following:                             <ul style="list-style-type: none"> <li>▪ Frequency: less than 15 headache days per month</li> <li>▪ No vomiting or nausea</li> <li>▪ No more than one of photophobia or phonophobia</li> </ul> </li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Chronic daily headache:</b> <ul style="list-style-type: none"> <li>○ Frequency: more than 15 days per month for more than 3 months</li> <li>○ Not a separate diagnosis</li> <li>○ A category of a primary or secondary headache disorder</li> </ul> </li> <li>• <b>Medication overuse headache:</b> <ul style="list-style-type: none"> <li>○ Frequency: 15 or more days per month</li> <li>○ Regular overuse for more than 3 months of one or more drugs for symptomatic treatment of headache:                             <ul style="list-style-type: none"> <li>▪ Ergotamine, triptans, opioids or combination analgesic medications on 10 or more days/month</li> <li>▪ Simple analgesics or any combination of ergotamine, triptans, analgesic opioids on 15 or more days/month, without overuse of any 1 class alone</li> </ul> </li> <li>○ Developed or worsened during medication overuse</li> </ul> </li> </ul>

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Appendix C – Headache Clinical Summary

<b>Prophylactic Treatment of Primary Headache</b>	
<ul style="list-style-type: none"> <li>• <b>Migraine prophylactic treatment:</b> <ul style="list-style-type: none"> <li>○ <b>Criteria:</b> <ul style="list-style-type: none"> <li>▪ Three or more severe migraines/month with inadequate response to symptomatic therapy</li> <li>▪ Less frequent but protracted attacks that impair patient's quality of life</li> <li>▪ Patient is interested in prophylactic treatment</li> </ul> </li> <li>○ <b>First-line treatment:</b> <ul style="list-style-type: none"> <li>▪ Beta blockers, calcium channel blockers, tricyclic antidepressants</li> <li>▪ Antiepileptics (divalproex, topiramate, gabapentin)</li> <li>▪ Patient education and lifestyle management</li> <li>▪ Screen for depression/anxiety</li> <li>▪ Other therapies available, but with varying levels of scientific support. Refer to complete guideline for this information</li> </ul> </li> <li>○ <b>Second-line treatment:</b> <ul style="list-style-type: none"> <li>▪ Different first-line med class or different drug of same class</li> <li>▪ Combination of beta blockers and tricyclics</li> </ul> </li> <li>○ <b>If menstrual-associated migraine:</b> <ul style="list-style-type: none"> <li>▪ Consider cyclic prophylaxis with NSAIDs (first choice), triptans, OR</li> <li>▪ Hormone prophylaxis (transdermal estradiol, estrogen-containing contraceptives)</li> <li>▪ Suppress menstrual cycle with GnRH agonist and "add back" therapy</li> </ul> </li> <li>○ <b>If menopausal or perimenopausal migraine:</b> <ul style="list-style-type: none"> <li>▪ Consider hormone therapy (oral or transdermal estrogen, progestin, or estrogen-containing contraceptives)</li> <li>▪ Therapy success defined as 50% reduction in headache frequency and/or severity</li> <li>▪ Hormone therapy may worsen migraines in some women</li> </ul> </li> <li>○ <b>If using or considering estrogen-containing contraceptives:</b> <ul style="list-style-type: none"> <li>▪ Evaluate vascular risk factors, such as risk for CAD, history of blood clots, migraine with aura, smoking</li> <li>▪ Risk of ischemic stroke increases with use of estrogen-containing contraceptives</li> <li>▪ Women with prolonged aura, or those who have an aura for the first time while using estrogen containing contraceptives, should be discouraged from using them.</li> </ul> </li> </ul> </li> <li>• <b>Tension-type headache prophylactic treatment</b> (more than 15 headaches/month):           <ul style="list-style-type: none"> <li>○ Amitriptyline and other tricyclic antidepressants; Venlafaxine XR</li> </ul> </li> </ul>	
<b>Treatment of Primary Headache</b>	
<ul style="list-style-type: none"> <li>• Early treatment of migraines, using effective medications, improves a variety of outcomes, such as duration, severity, and disability associated with chronic pain.</li> <li>• Long-term and first-line use of opiates and barbiturates should be avoided due to lack of studies to support effectiveness, side effects, and potential for abuse.</li> </ul>	
<ul style="list-style-type: none"> <li>• <b>Mild migraine treatment (self-management):</b> <ul style="list-style-type: none"> <li>○ APAP/ASA/Caffeine</li> <li>○ ASA alone</li> <li>○ Lidocaine nasal</li> <li>○ Midrin</li> <li>○ NSAIDs</li> <li>○ Triptans</li> </ul> </li> <li>• <b>Moderate migraine treatment:</b> <ul style="list-style-type: none"> <li>○ DHE (dihydroergotamine mesylate)</li> <li>○ Lidocaine nasal</li> <li>○ Midrin</li> <li>○ NSAIDs</li> <li>○ Triptans</li> </ul> </li> <li>• <b>Severe migraine treatment:</b> <ul style="list-style-type: none"> <li>○ Prochlorperazine</li> <li>○ Chlorpromazine</li> <li>○ DHE</li> <li>○ Ketorolac IM</li> <li>○ Magnesium Sulfate IV</li> <li>○ Triptans</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Adjunctive therapy for all migraines:</b> <ul style="list-style-type: none"> <li>○ Rest in quiet, dark room</li> <li>○ IV rehydration</li> <li>○ Antiemetics:               <ul style="list-style-type: none"> <li>▪ Hydroxyzine</li> <li>▪ Metoclopramide</li> <li>▪ Prochlorperazine</li> <li>▪ Promethazine</li> </ul> </li> <li>○ Caffeine</li> </ul> </li> <li>• <b>Cluster headache treatment:</b> <ul style="list-style-type: none"> <li>○ <b>Acute treatment:</b> <ul style="list-style-type: none"> <li>▪ Oxygen</li> <li>▪ Sumatriptan SQ (self-management)</li> <li>▪ Zolmitriptan nasal (self-management)</li> <li>▪ DHE</li> </ul> </li> <li>○ <b>Bridge treatment</b> (for quick suppression of attacks until maintenance treatment reaches therapeutic level):               <ul style="list-style-type: none"> <li>▪ Corticosteroids</li> <li>▪ Occipital nerve block</li> </ul> </li> <li>○ <b>Maintenance treatment</b> (for sustained suppression of attacks over the expected cluster cycle):               <ul style="list-style-type: none"> <li>▪ Avoid alcohol during cycle</li> <li>▪ Verapamil</li> <li>▪ Steroids</li> <li>▪ Lithium</li> <li>▪ Depakote</li> <li>▪ Topiramate</li> </ul> </li> </ul> </li> </ul>

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**Appendix C – Headache Clinical Summary**

<b>Treatment of Primary Headache (Continued)</b>	
<ul style="list-style-type: none"> <li>• <b>Status (lasting &gt; 72 hrs) treatment:</b> <ul style="list-style-type: none"> <li>○ DHE unless contraindicated. Must not be given within 24 hours of receiving any triptan or ergot derivative. Must not be used in patients with:                             <ul style="list-style-type: none"> <li>▪ Pregnancy</li> <li>▪ History of ischemic heart disease</li> <li>▪ History of variant angina</li> <li>▪ Severe peripheral vascular disease</li> <li>▪ Cerebrovascular disease</li> <li>▪ Hemiplegic or basilar-type migraine</li> <li>▪ Onset of chest pain following DHE test dose</li> </ul> </li> <li>○ If not DHE, then:                             <ul style="list-style-type: none"> <li>▪ Chlorpromazine</li> <li>▪ Valproate sodium IV</li> <li>▪ Magnesium Sulfate IV</li> <li>▪ Prochlorperazine</li> </ul> </li> <li>○ If treatment unsuccessful:                             <ul style="list-style-type: none"> <li>▪ Opiates (not meperidine)</li> <li>▪ Dexamethasone</li> </ul> </li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Tension-type headache treatment:</b> <ul style="list-style-type: none"> <li>○ <b>Acute treatment:</b> <ul style="list-style-type: none"> <li>▪ Acetaminophen</li> <li>▪ Aspirin</li> <li>▪ NSAIDs</li> <li>▪ Midrin</li> <li>▪ Avoid overuse of treatment meds</li> </ul> </li> </ul> </li> </ul>
<b>Self-Management of Primary Headache</b>	
<ul style="list-style-type: none"> <li>• <b>Potential migraine triggers to be avoided:</b> <ul style="list-style-type: none"> <li>○ Environmental--heat or cold, weather changes, flying or high altitude, bright lights, head or neck injury, odors</li> <li>○ Lifestyle--chronic stress, disturbed sleep, skipping meals or poor diet, smoking</li> <li>○ Hormonal--puberty, menstruation, pregnancy, menopause, oral contraceptives, estrogen therapy</li> <li>○ Emotional--anxiety, anger, depression, excitement, or "let down" response</li> <li>○ Dietary--citrus fruit, chocolate, aspartame, aged cheese, beer or red wine, caffeine, foods containing nitrates or MSG</li> <li>○ Medications--oral contraceptives, estrogen therapy, nifedipine, nitroglycerin</li> </ul> </li> <li>• <b>Patient education is especially important in the ongoing management of headache</b> <ul style="list-style-type: none"> <li>○ Most patients benefit from stress reduction, regular eating and sleeping schedules, and regular aerobic exercise</li> <li>○ Keeping a headache diary can help identify frequency, severity, triggers, and response to treatment</li> <li>○ The risk of chronic daily headaches is increased if headache treatment meds are used more than nine days a month</li> <li>○ Adherence to prophylactic treatment medications can lead to less frequent and less severe headache attacks</li> <li>○ It may not be possible to eliminate the primary headache completely</li> </ul> </li> </ul>	

\*Note: All information provided in this summary is for non-pregnant persons age 12 and over. Due to fetal risk and the complications of medication management, pregnant women, those who desire to become pregnant, or those who are breastfeeding should be treated based on the appropriate chronic pain and obstetrical guidelines.

\*\* Other disorders have been ruled out, or if another disorder is present, the headaches did not start around the same time as the disorder.

Used with permission by McKesson Health Solutions, 2012. The information contained in this Summary is based on the ICSI guideline and is not a comprehensive review.

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ICSI has long had a policy of transparency in declaring potential conflicting and competing interests of all individuals who participate in the development, revision and approval of ICSI guidelines and protocols.

In 2010, the ICSI Conflict of Interest Review Committee was established by the Board of Directors to review all disclosures and make recommendations to the board when steps should be taken to mitigate potential conflicts of interest, including recommendations regarding removal of work group members. This committee has adopted the Institute of Medicine Conflict of Interest standards as outlined in the report, *Clinical Practice Guidelines We Can Trust* (2011).

Where there are work group members with identified potential conflicts, these are disclosed and discussed at the initial work group meeting. These members are expected to recuse themselves from related discussions or authorship of related recommendations, as directed by the Conflict of Interest committee or requested by the work group.

The complete ICSI policy regarding Conflicts of Interest is available at <http://bit.ly/ICSICOI>.

### **Funding Source**

The Institute for Clinical Systems Improvement provided the funding for this guideline revision. ICSI is a not-for-profit, quality improvement organization based in Bloomington, Minnesota. ICSI's work is funded by the annual dues of the member medical groups and five sponsoring health plans in Minnesota and Wisconsin. Individuals on the work group are not paid by ICSI but are supported by their medical group for this work.

ICSI facilitates and coordinates the guideline development and revision process. ICSI, member medical groups and sponsoring health plans review and provide feedback but do not have editorial control over the work group. All recommendations are based on the work group's independent evaluation of the evidence.

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## **Disclosure of Potential Conflicts of Interest**

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Guideline Related Activities: None

Research Grants: None

Financial/Non-Financial Conflicts of Interest: Receives compensation from UpToDate as a headache document editor

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All ICSI documents are available for review during the revision process by member medical groups and sponsors. In addition, all members commit to reviewing specific documents each year. This comprehensive review provides information to the work group for such issues as content update, improving clarity of recommendations, implementation suggestions and more. The specific reviewer comments and the work group responses are available to ICSI members at <http://www.icsi.org/Headache>.

The ICSI Patient Advisory Council meets regularly to respond to any scientific document review requests put forth by ICSI facilitators and work groups. Patient advisors who serve on the council consistently share their experiences and perspectives in either a comprehensive or partial review of a document, and engaging in discussion and answering questions. In alignment with the Institute of Medicine's triple aims, ICSI and its member groups are committed to improving the patient experience when developing health care recommendations.

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## **Acknowledgements**

### **ICSI Patient Advisory Council**

The work group would like to acknowledge the work done by the ICSI Patient Advisory Council in reviewing the Diagnosis and Treatment of Headache and thank them for their suggestions on shared decision-making topics related to diagnosis, treatment options and side effects, and related patient education.

### **Invited Reviewers**

During this revision, the following groups reviewed this document. The work group would like to thank them for their comments and feedback.

HealthPartners Health Plan, Minneapolis, MN  
Lakeview Clinic, Waconia, MN  
Marshfield Clinic, Marshfield, WI  
Mayo Clinic, Rochester, MN  
Medica Health Plan, Hopkins, MN

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◀ The next revision will be no later than February 2018.

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## **ICSI Document Development and Revision Process**

### **Overview**

Since 1993, the Institute for Clinical Systems Improvement (ICSI) has developed more than 60 evidence-based health care documents that support best practices for the prevention, diagnosis, treatment or management of a given symptom, disease or condition for patients.

### **Audience and Intended Use**

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and other expert audiences.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients and families are urged to consult a health care professional regarding their own situation and any specific medical questions they may have. In addition, they should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in their individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition.

### **Document Development and Revision Process**

The development process is based on a number of long-proven approaches and is continually being revised based on changing community standards. The ICSI staff, in consultation with the work group and a medical librarian, conduct a literature search to identify systematic reviews, randomized clinical trials, meta-analysis, other guidelines, regulatory statements and other pertinent literature. This literature is evaluated based on the GRADE methodology by work group members. When needed, an outside methodologist is consulted.

The work group uses this information to develop or revise clinical flows and algorithms, write recommendations, and identify gaps in the literature. The work group gives consideration to the importance of many issues as they develop the guideline. These considerations include the systems of care in our community and how resources vary, the balance between benefits and harms of interventions, patient and community values, the autonomy of clinicians and patients and more. All decisions made by the work group are done using a consensus process.

ICSI's medical group members and sponsors review each guideline as part of the revision process. They provide comment on the scientific content, recommendations, implementation strategies and barriers to implementation. This feedback is used by and responded to by the work group as part of their revision work. Final review and approval of the guideline is done by ICSI's Committee on Evidence-Based Practice. This committee is made up of practicing clinicians and nurses, drawn from ICSI member medical groups.

### **Implementation Recommendations and Measures**

These are provided to assist medical groups and others to implement the recommendations in the guidelines. Where possible, implementation strategies are included that have been formally evaluated and tested. Measures are included that may be used for quality improvement as well as for outcome reporting. When available, regulatory or publicly reported measures are included.

### **Document Revision Cycle**

Scientific documents are revised every 12-24 months as indicated by changes in clinical practice and literature. ICSI staff monitors major peer-reviewed journals every month for the guidelines for which they are responsible. Work group members are also asked to provide any pertinent literature through check-ins with the work group midcycle and annually to determine if there have been changes in the evidence significant enough to warrant document revision earlier than scheduled. This process complements the exhaustive literature search that is done on the subject prior to development of the first version of a guideline.

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