



## Guideline Summary NGC-8275

### Guideline Title

**Managing chronic non-terminal pain in adults including prescribing controlled substances.**

### Bibliographic Source(s)

University of Michigan Health System. Managing chronic non-terminal pain in adults including prescribing controlled substances. Ann Arbor (MI): University of Michigan Health System; 2011 Jan. 36 p. [24 references]

### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Managing chronic non-terminal pain including prescribing controlled substances. Ann Arbor (MI): University of Michigan Health System; 2009 Mar. 34 p. [11 references]

### FDA Warning/Regulatory Alert

**Note from the National Guideline Clearinghouse:** This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [August 1, 2013 – Acetaminophen](#) : The U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients that acetaminophen has been associated with a risk of rare but serious skin reactions. Acetaminophen is a common active ingredient to treat pain and reduce fever; it is included in many prescription and over-the-counter (OTC) products. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever and pain/body aches (e.g., non-steroidal anti-inflammatory drugs, or NSAIDs, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions, which is already described in the warnings section of their drug labels.

### Scope

#### Disease/Condition(s)

Chronic non-terminal pain

#### Guideline Category

Diagnosis  
Management  
Treatment

#### Clinical Specialty

Anesthesiology  
Family Practice  
Internal Medicine  
Neurology  
Physical Medicine and Rehabilitation  
Rheumatology

#### Intended Users

Physicians

#### Guideline Objective(s)

To provide a systematic framework for providers to evaluate and manage patients with chronic, non-terminal pain with special attention to specific principles of opioid management

## Target Population

Adults with chronic non-terminal pain

## Interventions and Practices Considered

### Diagnosis

1. Pain history, including symptoms, initiating event, treatment, disability, psychiatric comorbidities, social stressors, barriers to care
2. Physical examination and radiologic studies
3. Assessment of opioid dependence and addiction risk

### Treatment/Management

1. Setting expectations
2. Non-pharmacologic therapies (e.g., exercise, heat, sleep hygiene)
3. Medical treatment, including:
  - Non-steroidal anti-inflammatory drugs (NSAIDs)
  - Adjuvant medications (tricyclic antidepressants [TCAs], serotonin-norepinephrine reuptake inhibitors [SNRIs], second generation anticonvulsants)
  - Opioid analgesics (morphine extended release, methadone, buprenorphine)
4. Follow-up frequency, assessment, and referral

## Major Outcomes Considered

- Extent of pain disability from chronic non-terminal pain
- Adverse effects of medication
- Proportion of patients with psychiatric comorbidities
- Proportion of patients with pain therapy addiction
- Proportion of patients requiring referral to comprehensive pain management

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

### Description of Methods Used to Collect/Select the Evidence

Preliminary evidence was identified using literature considered relevant in the Veterans Health Administration/Department of Defense (VA/DOD) clinical practice guideline for the management of opioid therapy. That report utilized literature searches from six earlier documents supplemented by a systematic literature search of publications from 1998 through July 2002.

A search of more recent literature was conducted on Medline prospectively using the major keywords of: *chronic pain non-malignant, human, English language, clinical trials, guidelines, and published from 1/1/00 through 1/15/10*. For some specific topics (noted below) the timeframe was extended to include publications from 1/1/95 through 4/15/05. Terms used for specific topic searches within the major key words included: *pain assessment, opioids (since 1995), other drugs (e.g., NSAIDs, acetaminophen, muscle relaxants, tricyclics, gabapentin; since 1995), physical therapy (since 1995), psychological interventions (since 1995), multidisciplinary treatment (since 1995), other non-pharmacologic treatment (since 1995), pain reassessment and monitoring, psychiatric comorbidities (e.g., personality disorders, history of substance abuse; since 1995), vulnerable populations (e.g., elderly, poor, minorities, pediatrics, disabled, psychiatric; since 1995), legal issues with opioids, prevention of opioid abuse, monitoring opioid use, opioid abusing patients, discontinuing prescribing opioids and discharging patients*. Detailed search terms and strategy available upon request from the guideline developer.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with recent information available to expert members of the panel, including abstracts from recent meetings and results of clinical trials. Negative trials were specifically sought. The search was a single cycle.

### Number of Source Documents

Not stated

### Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

### Levels of Evidence

- A. Randomized controlled trials
- B. Controlled trials, no randomization
- C. Observational trials
- D. Opinion of expert panel

### Methods Used to Analyze the Evidence

Systematic Review

### Description of the Methods Used to Analyze the Evidence

Consensus of the guideline team after reviewing the evidence and discussion.

### Methods Used to Formulate the Recommendations

Expert Consensus

### Description of Methods Used to Formulate the Recommendations

Conclusions were based on prospective randomized controlled trials (RCTs) if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

### Rating Scheme for the Strength of the Recommendations

#### Strength of Recommendation

- I. Generally should be performed
- II. May be reasonable to perform
- III. Generally should not be performed

### Cost Analysis

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

### Method of Guideline Validation

Comparison with Guidelines from Other Groups

Internal Peer Review

### Description of Method of Guideline Validation

This guideline is consistent with the Veterans Health Administration, Department of Defense (VA/DOD) Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. It is also consistent with the Clinical Guidelines for the Use of Chronic Opioid Therapy I Chronic Noncancer Pain of the American Pain Society – American Academy of Pain Medicine Opioids Guidelines Panel.

University of Michigan Health System (UMHS) guidelines are reviewed by leadership and in clinical conferences of departments to which the content is most relevant. This guideline was reviewed by the Department of Anesthesiology, the Department of Family Medicine, the Division of General Medicine, the Division of Geriatric Medicine, and the Department of Physical Medicine & Rehabilitation.

## Recommendations

### Major Recommendations

**Note from the University of Michigan Health System (UMHS) and the National Guideline Clearinghouse (NGC):** The following guidance was current as of January 2011. Because UMHS occasionally releases minor revisions to its guidance based on new information, users may wish to consult the [original guideline document](#) for the most current version.

**Note from NGC:** The following key points summarize the content of the guideline. Refer to the full text of the original guideline document for additional information, including detailed information on the evaluation and management of chronic pain and selected medications for chronic pain.

The levels of evidence [A-D] and strength of recommendation [I-III] are defined at the end of the "Major Recommendations" field.

#### Diagnosis

Chronic pain is different from acute pain. It requires comprehensive physical, functional, behavioral and psychosocial assessment.

- **History.** Pain history should include a detailed description of symptoms, initiating injury or event, detailed treatment history, pain-related disability, psychiatric comorbidity, social stressors and barriers to care (e.g., insurance, education, pharmacy access, support systems). [ID]

From and laboratory findings. Physical exam, findings, and radiographic studies may identify opportunities for

- **Exam and laboratory findings.** Physical exam findings and radiographic studies may identify opportunities for procedural interventions or surgery, but these findings often do not correlate with symptom severity, degree of disability or appropriate intensity of treatment. [IID]
- **Opioids and addiction risk.** If opioid analgesics have been used or are being considered, dependence and addiction risk should be assessed through careful personal and family history, review of outside records, and assessment of illicit or prescription medication misuse. Check your State's prescription monitoring program (PMP) and perform a urine screen by combination of enzyme immunolinked assay (EIA) and gas chromatography/mass spectroscopy (GCMS) prior to prescribing and at least yearly for patients given chronic opioid therapy. [ID]

### Treatment

Treatment must be multi-dimensional, not only pharmacological. Effective therapy should control chronic pain in order to improve function at work, home, socially and in pleasurable pursuits. Complete analgesia is not possible for many patients.

- **Expectations.** Patient and provider expectations should be articulated clearly at the beginning of treatment and reviewed regularly. A written controlled substance treatment agreement is appropriate for most patients treated with ongoing daily opioid therapy. [ID]
- **Non-pharmacologic therapies.** Begin with these therapies (e.g., exercise, heat, sleep hygiene).
- **Medical treatment.** Choose drugs based on presumed pain type and the patient's comorbidities.
  - **Non-steroidal anti-inflammatory drugs (NSAIDs)** and/or acetaminophen can be effective for chronic musculoskeletal or arthritis pain. In older adults, non-steroidal anti-inflammatory drugs and cyclooxygenase-2 (COX-2) inhibitors should be used rarely and with caution, monitoring for gastrointestinal (GI) and renal toxicity, hypertension, and heart failure. [ID]
  - **Adjuvant medications** Tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs) (duloxetine) and second generation anticonvulsant medications are effective for specific neuropathic pain states. [IA] For centralized pain/fibromyalgia, TCAs, SNRIs, gabapentin and pregabalin are effective. [IA]
  - **Opioid analgesics** can be safe and effective for *some* patients with chronic non-terminal pain [IIB], but require careful patient selection, titration and monitoring. Scheduled, long-acting opioids (morphine extended-release [ER], or methadone, buprenorphine) are preferred for continuous treatment [ID]. *OxyContin* has a higher risk for misuse or diversion. Avoid long-term, daily treatment with short-acting opioids and opioid combinations (e.g., *Vicodin, Norco, Percocet*). For "as needed" (PRN) dosing, prescribe small amounts expecting monthly (not daily) use.

### Follow-up

Reassessment should center on achieving shared treatment goals and improved function.

- **Frequency.** Patients should be seen frequently (weekly to monthly) during initial evaluation and treatment, and at least quarterly thereafter. [ID]
- **Assessment.** Reassess physical, psychological and social domains regularly, particularly progress toward improved function. [ID]
- **Ineffective treatments.** Stop ineffective treatment modalities (e.g., non-steroidal anti-inflammatory drugs, opioids). [ID]
- **Opioids and problem use.** Monitor patients receiving opioid analgesics for misuse with checks of State registries (PMP) for prescription fills (e.g., in Michigan called Michigan Automated Prescribing Service [MAPS]) and random urine comprehensive drug screens by enzyme immunolinked assay and gas chromatography/mass spectroscopy (EIA-GCMS). [IID]
- **Referral.** Referral to pain management specialist should be considered for failure to achieve treatment goals, intolerance of therapies, need for interventional management, need for multidisciplinary treatment, need for excessive opioid doses, suspicion of addiction, or opioid misuse. [IB]

### Definitions:

#### Levels of Evidence

- A. Randomized controlled trials
- B. Controlled trials, no randomization
- C. Observational trials
- D. Opinion of expert panel

#### Strength of Recommendation

- I. Generally should be performed
- II. May be reasonable to perform
- III. Generally should not be performed

### Clinical Algorithm(s)

None provided

### Evidence Supporting the Recommendations

#### Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is specifically stated and graded for each recommendation (see the "Major Recommendations" field).

Conclusions were based on prospective randomized controlled trials (RCTs) if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Appropriate management of chronic non-terminal pain
- Improvement or maintenance of acceptable levels of pain disability

### Potential Harms

#### Drug Side Effects

- Although acetaminophen is generally safe and well-tolerated by most patients, excessive doses can cause severe or even fatal hepatic injury. Older adults and patients with active liver disease or increased risk (e.g., concurrent carbamazepine, zidovudine, isoniazid, or high-dose phenytoin administration; heavy alcohol use; cachexia, etc.) should be monitored closely while taking acetaminophen regularly. Such patients should be limited to a total of 3 grams daily.
- Chronic nonsteroidal anti-inflammatory drug (NSAID) use also poses significant risks for gastrointestinal bleeding, renal insufficiency and platelet dysfunction. Hazards are magnified for patients with known peptic ulcer disease, renal insufficiency, bleeding dyscrasias, congestive heart failure and concurrent corticosteroid therapy, among others. Age is a particular risk: older adults receiving daily NSAIDs for six months or more face a 6 to 9 percent risk for gastrointestinal (GI) bleeding requiring hospitalization. NSAIDs also increase risk for exacerbations of hypertension, heart failure, and renal dysfunction.
- While cyclooxygenase-2 (COX-2) inhibitors demonstrated lower GI risk compared to traditional NSAIDs, subsequent studies have shown increased cardiovascular risk with ongoing COX-2 use. Subsequently, manufacturers of COX-2 selective NSAIDs have either significantly modified labeling for these medications or withdrawn them altogether. Older patients treated with COX-2 inhibitors and aspirin together should be given gastrointestinal protection with a proton pump inhibitor.
- While the first-generation anticonvulsants like phenytoin (Dilantin) and carbamazepine (Tegretol) have shown some efficacy for neuropathic pain, they are associated with frequent side effects, drug-drug interactions, and potentially severe adverse reactions. Second generation agents such as gabapentin (Neurontin), topiramate (Topamax), and pregabalin (Lyrica) are also effective in treating neuropathic pain and generally better-tolerated, though they can be significantly more expensive, more complex to dose, and still pose significant adverse risk.
- Benzodiazepines should not be routinely prescribed for patients with chronic pain, as they carry independent and complicating risks for tolerance, misuse, and addiction.
- With prolonged use in some patients, opioids can become ineffective and, at more than minimal doses, *lower* pain threshold and induce hyperalgesia. Concerns about the use of opioids are many, and are shared by providers and patients alike. These are drugs with potentially serious adverse effects and complications including drug abuse, addiction and diversion for sale. Unscrupulous and/or poorly supervised use of these medications can lead patients down a path to inappropriate use, often does not lead to desired outcomes, and creates ethical dilemmas and legal risks for providers. However, excessive fear of and reluctance to use these medications can lead to their under use, preventing effective therapy of chronic pain.
- Mild to moderate side effects to opioids are as common as 50% to 66%. The most common adverse effects are sedation, nausea, headache, pruritus, and constipation. Other effects can be confusion, hallucinations, nightmares, urinary retention, dizziness and headache. Tolerance and regression of most side effects often occur quickly. Constipation and urinary retention (smooth muscle inhibitory effects) are more persistent.
- Nausea may be a bit more common with codeine while constipation may be a bit worse with oxycodone and rash may be more common with morphine. Otherwise, most opioids are very similar.
- Respiratory depression may occur with high dose administration to opioid naïve patients. It is the most serious potential adverse effect, and is accompanied by symptoms of sedation and confusion. Opioids, at therapeutic doses, depress respiratory rate and tidal volume. As carbon dioxide (CO<sub>2</sub>) rises, central chemoreceptors cause a compensatory increase in respiratory rate. Patients with impaired ventilatory reserve (chronic obstructive pulmonary disease [COPD], asthma) are therefore at greater risk of clinically significant respiratory depression. Tolerance to respiratory depression develops within just a few days.
- Cognitive function, including the ability to drive, is preserved when on stable, moderate doses of opioids. Cognitive impairment may occur temporarily after an increase in dose. Tolerance to cognitive effects usually develops quickly.
- The long-term use of opioids, particularly in doses above those typically prescribed for pain, may be associated with the development of an increased sensitivity to pain (opioid-induced hyperalgesia). This may be one mechanism of "apparent opioid tolerance" along with true pharmacologic tolerance and disease progression. Fortunately, tolerance to the analgesic effect, when it does occur, develops much more slowly than tolerance to these adverse effects.
- Patients with continued uncontrolled pain on high doses of opioids will likely require detoxification, often via buprenorphine (Suboxone®). This drug may be prescribed only by physicians and certified pain specialists experienced in its use.

## Contraindications

### Contraindications

- Contraindications for initiating or continuing chronic opioid therapy are:
  - Central pain syndrome — opioid not indicated

• History of prescription drug abuse, evidence of diversion of controlled substances, illegal activities with prescriptions

- Forgery of prescriptions, evidence of diversion of controlled substances, illegal activities with prescriptions
- Biochemical abnormalities have been demonstrated in fibromyalgia patients, including increased pronociceptive neuropeptides and excitatory amino acids in the cerebrospinal fluid (CSF) (e.g., Substance P, glutamate) and decreased concentrations and activity of antinociceptive substances (e.g., serotonin, norepinephrine). In light of this, one could conclude that chronic opioid therapy may be contraindicated in these patients.

## Qualifying Statements

### Qualifying Statements

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Chart Documentation/Checklists/Forms

Patient Resources

Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Living with Illness

### IOM Domain

Effectiveness

Patient-centeredness

Safety

## Identifying Information and Availability

### Bibliographic Source(s)

University of Michigan Health System. Managing chronic non-terminal pain in adults including prescribing controlled substances. Ann Arbor (MI): University of Michigan Health System; 2011 Jan. 36 p. [24 references]

### Adaptation

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

### Date Released

2009 Mar (republished 2011 Jan)

### Guideline Developer(s)

University of Michigan Health System - Academic Institution

### Source(s) of Funding

University of Michigan Health System

### Guideline Committee

Chronic Pain Management Guideline Team

### Composition of Group That Authored the Guideline

*Team Leads:* Daniel W Berland, MD, General Medicine/Anesthesiology; Phillip E Rodgers, MD, Family Medicine

*Team Members:* Carmen R Green, MD, Anesthesiology; R Van Harrison, PhD, Medical Education; Randy S Roth, PhD, Physical Medicine & Rehabilitation

*Consultants:* Daniel J. Clauw, MD, Rheumatology; Jennifer A. Meddings, MD, General Medicine; Ronald A Wasserman, MD, Anesthesiology

*UMHS Guidelines Oversight Team:* Connie J Standiford, MD; William E Chavey, MD; R Van Harrison, PhD

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#### Team Member; Company; Relationship:

Daniel W. Berland, MD (none)

Daniel J. Clauw, MD; Consultant; Cypress Bio-sciences, Forest, Lilly, Pfizer, Pierre Fabre, Takeda, UCB; Research funding; Cypress Bio-sciences, Forest

Carmen R. Green, MD (none)

R. Van Harrison, PhD (none)

### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Managing chronic non-terminal pain including prescribing controlled substances. Ann Arbor (MI): University of Michigan Health System; 2009 Mar. 34 p. [11 references]

### Guideline Availability

Electronic copies: Available from the [University of Michigan Health System Web site](#).

### Availability of Companion Documents

Continuing Medical Education (CME) information is available from the [University of Michigan Health System Web site](#).

Additional implementation tools, including pain assessment tools, outlines for evaluation, an opioid risk tool, a patient-provider agreement form for ongoing use of controlled medication, and an example clinical policy on long-term controlled substances are available in the appendices to the [original guideline document](#).

### Patient Resources

The following is available:

- Chronic pain. Ann Arbor (MI): University of Michigan Health System; 2009 Jun. Various p. Electronic copies: Available from the [University of Michigan Health System Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

### NGC Status

This NGC summary was completed by ECRI Institute on November 25, 2009. The information was verified by the guideline developer on December 21, 2009. This summary was updated by ECRI Institute on July 26, 2010 following the U.S. Food and Drug Administration (FDA) advisory on Proton Pump Inhibitors (PPI). This NGC summary was updated by ECRI Institute on April 19, 2011. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen.

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