

# CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

## Part 1: Introduction

The chronic pain medical treatment guidelines apply when the patient has chronic pain as determined by following the clinical topics section of the Medical Treatment Utilization Schedule (MTUS). In following the clinical topics section, the physician begins with an assessment of the presenting complaint and a determination as to whether there is a “red flag for a potentially serious condition” which would trigger an immediate intervention. Upon ruling out a potentially serious condition, conservative management is provided and the patient is reassessed over the next 3-4 weeks. If the complaint persists during this interval, the physician needs to reconsider the diagnosis and decide whether a specialist evaluation is necessary. The chronic pain medical treatment guidelines apply to patients who fail to recover and continue to have persistent complaints without definitive treatment, such as surgical options. This provides a framework to manage all chronic pain conditions, even when the injury is not addressed in the clinical topics section of the MTUS.

The chronic pain medical treatment guidelines consist of two parts. Part 1 is the introduction. Part 2 consists of pain interventions and treatments. With a few exceptions, Part 2 is primarily an adaptation of evidence-based treatment guidelines, from the Work Loss Data Institute’s Official Disability Guidelines (ODG) Treatment in Workers’ Comp – Chapter on Pain (Chronic). The version adapted is dated October 31, 2007, and it is being adapted with permission from the ODG publisher. Any section not adapted directly from ODG is labeled “[DWC]”.

### Definitions:

**Chronic Pain:** Chronic pain is defined as “*any pain that persists beyond the anticipated time of tissue healing.*”

**Types of Pain:** Pain mechanisms can be broadly categorized as nociceptive or neuropathic.

**Nociceptive pain:** Nociceptive pain is the pain caused by activation of nociceptors, which are sensory neurons found throughout the body. A nociceptor is “a receptor preferentially sensitive to a noxious stimulus or to a stimulus which would become noxious if prolonged.”

**Neuropathic Pain:** Neuropathic pain is “pain initiated or caused by a primary lesion or dysfunction of the nervous system.” Normal nociception would not be considered dysfunction of the nervous system.

### Overview

Chronic pain has a huge impact on the individual and society as a whole. It is the primary reason for delayed recovery and costs in the workers’ compensation system. Most chronic pain problems start with an acute nociceptive pain episode. Therefore, effective early care is paramount in preventing chronic pain. Given the importance of pain in healthcare, it is presently the subject of intensive scientific research which in turn has generated a growing evidence base regarding the diagnosis, treatment and management of painful conditions.

The International Association for the Study of Pain (IASP) states that pain is “*an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such*”

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*damage.*” (Merskey and Bugduk 1994) This describes pain as a subjective experience; therefore, unlike hypertension or diabetes, there is no objective measurement for pain intensity. Analysis of the objective data (psychosocial assessment, physical exam findings, imaging results, lab tests) is needed to evaluate the patient’s subjective report of pain.

The experience of pain is a complex phenomenon. Multiple models have evolved over time to explain it. Traditionally, the biomedical model explains pain through etiologic factors (e.g. injury) or disease whose pathophysiology results in pain. It is now understood that this classic biomedical approach to understanding and treating pain is incomplete. Its exclusive application can result in unrealistic expectations on the part of the physician and patient, inadequate pain relief, and excessive disability in those with pain that persists well after the original injury has healed.

The biopsychosocial model of pain instead recognizes that pain is ultimately the result of the pathophysiology plus the psychological state, cultural background/belief system, and relationship/interactions with the environment (workplace, home, disability system, and health care providers). Current research is investigating the neurobiological causes for persistent pain and how structural and functional changes in the central nervous system may serve to amplify and maintain the experience and disability of certain pain condition. (Siddall and Cousins 2007) This is an area of intensive research which will contribute to the scientific evidence base in years to come.

## Pain Mechanisms

Within the biomedical model, pain mechanisms are broadly categorized as nociceptive or neuropathic. Inflammatory mechanisms may also play a role. While there are similarities, each mechanism has unique features and characteristics. This mechanistic approach may provide greater insight into appropriate therapeutic strategies.

Several reviews have detailed the mechanisms and mediators of pain and the components of the ascending and descending pain pathways. In nociceptive pain, signal transduction in nociceptor somatosensory afferent terminals converts mechanical, electrical, thermal, or chemical energy into an action potential which is transmitted to the dorsal horn of the spinal cord by specialized nerve fibers. The signal is then transmitted through ascending cortical pathways to the brain. Nociceptive signals within the brain are sent to two major areas: the somatosensory cortex, where the sensory component of pain is represented in the brain, and the limbic forebrain system, which is the neural substrate for the emotional component of pain experience responsible for feelings of suffering.

Since these areas of the brain interact with other areas of the brain, past memories, external environmental factors, and internal cognitive factors (i.e. psychosocial factors) influence or modulate the pain experience. How the brain integrates all the input is, in part, the basis for the biopsychosocial approach to the management of pain.

Neuropathic pain is “pain initiated or caused by a primary lesion or dysfunction of the nervous system.” (Turk and Okifuji 2001) The altered modulation of the pain response in patients with neuropathic pain causes a state of hyperexcitability and continuous pain signal output in the absence of peripheral tissue damage. “Neuropathic pain can result from injury or trauma (e.g. surgery), infection (e.g. post herpetic neuralgia), endocrine (e.g. diabetes, hypothyroidism), demyelination (e.g. multiple sclerosis), errors in

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metabolism, neurodegenerative disorders (e.g. Parkinson's disease), or damage directly to the spinal cord or brain (e.g. thalamic stroke).’ (Backonja in Loeser, 2001)” (Mackey and Maeda 2004)

Neuropathic pain is characterized by lancinating, paroxysmal, tingling, and burning sensations that are distinct from nociceptive pain.

Many neuropathic pain states have traditionally been thought of as having a primary peripheral etiology. Recent investigation, however, using functional neuroimaging techniques, demonstrates that many neuropathic and other chronic pain conditions may have a large centralized component (central vs. peripheral model). These conditions include chronic low back pain (CLBP), fibromyalgia, irritable bowel syndrome, and Complex Regional Pain Syndrome (CRPS)/Reflex Sympathetic Dystrophy (RSD). (Mackey and Maeda 2004)

Inflammation can play a significant role in both nociceptive and neuropathic pain. Inflammation occurs when cells and tissue are damaged and release chemical mediators, commonly referred to as “the inflammatory soup,” that not only induce an inflammatory response but also sensitize nociceptors and other somatosensory components of the nervous system. Peripheral sensitization occurs when inflammatory mediators cause a reduction in the threshold required for nociceptor activation. A similar short-term central sensitization can occur in which there is an increase in neuronal excitability and responsiveness in the dorsal horn. In central sensitization, chemical mediators for inflammation can also upregulate the expression of genes that alter synaptic transmission.

Because of neuronal plasticity, current research is showing that protracted central sensitization (neuronal hyperexcitability) can result in long-term changes that may be important in the transition from acute to chronic pain and the development of chronic pain syndromes. Patients with these syndromes generally have severe and persistent pain that is disproportionate to the tissue injury.

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## Models

Models are the conceptual framework for physicians, patients, families, healthcare facilities, carriers, and compensation systems for understanding pain. Models help to establish parameters for reasonable outcomes and acceptable standards of care. Several different models of pain have developed over time, each with insights and limitations.

### Acute vs. Chronic Pain Model

In many situations, acute pain serves as a highly adaptive and beneficial experience. Fundamentally, it serves as a warning of actual or impending tissue damage. Acute musculoskeletal pain is a common example in the injured worker and is often a signal of real or impending tissue damage.

Most acute pain is self-limited or responds to short term administration of analgesics and conservative therapies. However, continued activation of nociceptors with poor pain control can lead to peripheral and central sensitization, a risk factor for persistent pain leading to a neuropathic pain state with prolonged disability, delayed return to baseline function, and delayed return to work.

Chronic pain can be distinguished from acute pain by more than just the time course. Whereas acute pain serves as a warning signal, chronic pain has no known survival benefit. Chronic pain is persistent and relentless, serving no obvious purpose for the individual. Evidence suggests that generation and subsequent maintenance of chronic pain, as opposed to acute pain, involves changes in central pain processing mediated through mechanisms of neural plasticity and ultimately leading to hyper-excitability of central structures in the spinal cord and brain. To complicate matters, unremitting pain may be associated with depression or anxiety.

As a practical matter, it is noted that “[t]he distinction between acute and chronic pain is somewhat arbitrary” and “[c]hronicity may be reached from one to six months postinjury”, ACOEM recognizes that the most clinically useful definition might be “chronic pain persists beyond the usual course of healing of an acute disease or beyond a reasonable time for an injury to heal”. (ACOEM Medical Treatment Guidelines Chapter 6 page 108). Therefore, it is a clinical decision to recognize chronicity or persistence of pain when 1) the condition is not improving over time, 2) fails to improve with treatments directed to the specific injured body part (see Clinical Topics section of the MTUS), 3) or in the absence of a specifically correctable anatomic lesion (see Clinical Topics section of the MTUS). Often it takes a number of months for the clinician to recognize when pain becomes chronic.

### Illness Behavior Model

As previously stated pain is a subjective experience, influenced and modulated by cognitive, emotional, and environmental elements. Psychosocial factors can affect the perception and expression of pain. These might include a tendency toward anxiety, depression, somatization, fear avoidance, emotional lability, catastrophizing, job dissatisfaction and embellishment.

Further, while frank malingering is rare, secondary gain factors, such as disability income and avoidance of perceived unpleasant tasks can impact the overall clinical presentation. Taken together, psychosocial factors may play a larger role in eventual patient outcome than obvious somatic factors as determined by

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the nature and extent of the original injury. Efforts directed solely to the management of possible pain generators without addressing psychosocial factors may result in a suboptimal outcome.

## Biomedical vs. Biopsychosocial Model

The traditional biomedical model “assumes disease to be fully accounted for by deviations from the norm of measurable biological (somatic) variables” (Engel 1977). Thus there is always a direct causal relationship between a specific pathophysiologic process and the presence and extent of a particular symptom. While this model has served the medical community well in the treatment and cure of certain diseases (e.g. infectious diseases), it has generally failed in the treatment of chronic illness including persistent pain. For example, for decades there has been an approach to identify the “pain generator” and remove it by cutting it out or blocking it.

In 1977 Engel proposed an alternative, the biopsychosocial model, which focuses greater attention on the patient, rather than presumed pathophysiology. The biopsychosocial model approaches pain and disability as a complex interplay of biological, psychological and social factors. These psychosocial factors can be easily assessed.

The following chart contrasts these two pain models (Hanson and Gerber 1993).

### **Pain Models**

<b>Biomedical model</b>	<b>Biopsychosocial model</b>
Most appropriate for acute pain conditions	More useful for those with chronic pain conditions
Emphasizes peripheral nociception	Recognizes the role that central mechanisms play in modulating peripheral nociception or generating the experience of pain in the absence of nociception
Focus on physical disease mechanisms	Recognizes the importance of illness behavior including cognitive and emotional responses to pain
Reductionistic approach to understanding and treating pain	Multidimensional systems approach to understanding and treating pain
Reliance on medical management approaches	Utilization of self-management approaches

Linton, when discussing the psychosocial risk factors involved in the creation of chronic back and neck pain, noted that “there is strong evidence that psychosocial variables are strongly linked to the transition from acute to chronic pain disability.” He stated “there is strong evidence that psychosocial variables generally have more impact than biomedical or biomechanical factors on back pain disability.” Thus, when clinical progress is insufficient, the clinician should always be prepared to address confounding psychosocial variables, in a coordinated, multidisciplinary manner.

## Medical vs. Self-Management Model

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Understandably, patients want their chronic pain cured or eliminated. Unfortunately, there are presently no definitive cures for the majority of persistent pain problems, such as axial spine pain, peripheral neuropathies, fibromyalgia, etc. As is the case with all chronic medical conditions, chronic pain must be managed, not cured. In the medical model, responsibility resides primarily with the physician. The self-management approach places primary responsibility on the person with chronic pain. Currently, self-management strategies can significantly improve a patient's function and quality of life, while reducing subjective experiences of pain. It is important to educate patients on this distinction, to avoid persistent and unrealistic expectations for an elusive cure, where none exists. This unrealistic curative view, often unwittingly fostered by healthcare providers or others, predictably leads to repeated failure, delayed recovery, and unnecessary disability and costs.

## **Risk Stratification**

### Importance of early identification

Patients not responding to initial or subacute management ( see Clinical Topics Section MTUS) or those thought to be at risk for delayed recovery should be identified as early as possible. Simple screening questionnaires may be used early in the clinical course to identify those at risk for delayed recovery. Those at risk should be aggressively managed to avoid ineffective therapeutic efforts and needless disability. Factors that help identify at-risk patients include: (1) those unresponsive to conservative therapies demonstrated to be effective for specific diagnoses; (2) significant psychosocial factors negatively impacting recovery; (3) loss of employment or prolonged absence from work; (4) previous history of delayed recovery or rehabilitation; (5) lack of employer support to accommodate patient needs; and (6) a history of childhood abuse (verbal, physical, mental). Of these factors, lost time from work has the highest value in predicting those patients who will experience delayed recovery.

### Subacute Delayed Recovery

Complaints of pain are the most common obstacle to return to work. Undertreatment of pain and/or unrealistic expectations may play a role in delayed recovery. However, the subacute phase is a critical time for the injured worker, as additional time away from work may result in adverse medical, familial, economic, and psychological consequences (including overtreatment, depression and/or anxiety, which can exacerbate pain complaints). When the physician recognizes that the problem is persisting beyond the anticipated time of tissue healing, the working diagnosis and treatment plan should be reconsidered, and psychosocial risk factors should be identified and addressed. Patients should be directed toward resources capable of addressing medical and psychosocial barriers to recovery.

### Patients with Intractable Pain

Studies have shown that the longer a patient remains out of work the less likely he/she is to return. Similarly, the longer a patient suffers from chronic pain the less likely treatment, including a comprehensive functional restoration multidisciplinary pain program, will be effective. Nevertheless, if a patient is prepared to make the effort, an evaluation for admission for treatment in a multidisciplinary treatment program should be considered.

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A patient suffering from severe intractable pain who does not qualify for participation in a chronic pain program or who has failed a chronic pain program “should have access to proper treatment of his or her pain.” California Health and Safety Code section 124960

## **Assessment Approaches**

### History and Physical Examination

Thorough history taking is always important in clinical assessment and treatment planning for the patient with chronic pain. Clinical recovery may be dependent upon identifying and addressing previously unknown or undocumented medical and/or psychosocial issues. Diagnostic studies should be ordered in this context and not simply for screening purposes.

If a diagnostic workup is indicated and it does not reveal a clinically significant contraindication, the physician should encourage the patient to engage in an active rehabilitation program. Effective treatment of the chronic pain patient requires familiarity with patient-specific past diagnoses, treatment failures/successes, persistent complaints and confounding psychosocial variables (e.g. history of abuse, anxiety, depression, fear-based avoidance of activity, catastrophizing, self-medication with alcohol or other drugs, patient/family expectations, medical-legal/claims management issues, and employer/supervisor/worksites).

A thorough physical examination is also important for establishing reassurance and patient confidence, establishing/confirming diagnoses, and observing/understanding pain behaviors

### Evaluation of Psychosocial Factors

For patients with a complex presentation, psychosocial factors have proven better predictors of chronicity than clinical findings. Such variables/factors can and should be assessed.

## **Functional Restoration Approach to Chronic Pain Management**

Many injured workers require little treatment, and their pain will be self-limited. Others will have persistent pain, but can be managed with straightforward interventions and do not require complex treatment. However, for patients with more complex or refractory problems, a comprehensive multidisciplinary approach to pain management that is individualized, functionally oriented (not pain oriented), and goal-specific has been found to be the most effective treatment approach. (Flor, Fydrich et al. 1992; Guzman, Esmail et al. 2001; Gatchel and Bruga 2005)

Functional restoration is an established treatment approach that aims to minimize the residual complaints and disability resulting from acute and/or chronic medical conditions. Functional restoration can be considered if there is a delay in return to work or a prolonged period of inactivity according to ACOEM Practice Guidelines, 2<sup>nd</sup> Edition, page 92. Functional restoration is the process by which the individual acquires the skills, knowledge and behavioral change necessary to avoid preventable complications and assume or re-assume primary responsibility (“locus of control”) for his/her physical and emotional well-being post injury. The individual thereby maximizes functional independence and

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pursuit of vocational and avocational goals, as measured by functional improvement (see 8 CCR § 9792.20 (f)).

Independent self-management is the long-term goal of all forms of functional restoration. The process and principles of functional restoration can be applied by a physician or a well integrated interdisciplinary team to a full range of problems that include acute injuries (e.g., sports, occupational), catastrophic injuries (e.g., brain and spinal cord injury), and chronic conditions (e.g., chronic pain, multiple sclerosis, etc.) and is the basis for medical rehabilitation and disability management. The principles of functional restoration apply to all conditions in general, and are not limited to injuries or pain.

Multiple treatment modalities, (pharmacologic, interventional, psychosocial/behavioral, cognitive, and physical/occupational therapies) are most effectively used when undertaken within a coordinated, goal-oriented, functional restoration approach (see Part 2).

Using medications in the treatment of pain requires a thorough understanding of the mechanism underlying the pain as well as to identify comorbidities that might predict an adverse outcome. As stated on page 47 of the ACOEM Practice Guidelines, “[c]onsideration of comorbid conditions, side effects, cost, and efficacy of medication versus physical methods and provider and patient preferences should guide the physician’s choice of recommendations.” Choice of pharmacotherapy must be based on the type of pain to be treated and there may be more than one pain mechanism involved. When effective, medications provide a degree of analgesia that permits the patients to engage in rehabilitation, improvement of activities of daily living, or return to work. There are no drugs that have been proven to reverse, cure, or “heal” chronic pain or neuropathic. Periodic review of the ongoing chronic pain treatment plan for the injured worker is essential according to the Medical Board of California Pain Guidelines for controlled substances.

When choosing an invasive procedure to treat a specific chronic pain problem, a complex judgment is necessary to make sure that the desired and expected outcome is worth the risk involved, depending on the procedure and individual risk factors.

Please refer to Part 2 to find specific guidelines on chronic pain treatments that include pharmacotherapy, invasive pain procedures, psychological and behavioral therapies, physical and occupational therapies, and other approaches. Whether the treatment is provided by an individual provider, a multidisciplinary group of providers, or tightly integrated interdisciplinary pain program, it is important to design a treatment plan that explains the purpose of each component of the treatment. Furthermore, demonstration of functional improvement is necessary at various milestones in the functional restoration program in order to justify continued treatment.

## **Pain Outcomes and Endpoints**

Pain is subjective. It cannot be readily validated or objectively measured (AMA Guides, 5<sup>th</sup> Edition, page 566). Furthermore subjective reports of pain severity may not correlate well with its functional impact. Thus, it is essential to understand the extent that function is impeded by pain (AMA Guides, 5<sup>th</sup> Edition, page 578). Moreover, “[t]he desired end point in pain management is return to function rather than complete or immediate cessation of pain.” (ACOEM Practice Guidelines, 2<sup>nd</sup> Edition, p. 116)

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Physicians treating in the workers' compensation system must be aware that just because an injured worker has reached a permanent and stationary status or maximal medical improvement does not mean that they are no longer entitled to future medical care.

## Conclusion

We now have an appreciation that neuropathic pain is associated with structural and functional changes of the peripheral and central nervous system. These changes can lead to the generation and maintenance of chronic pain conditions with its associated disability. While biologic mechanisms play a role in the perception of pain, it is also important to recognize that psychological and environmental factors are important. Recognition of these factors will allow the physician to better (1) treat the recently injured patient, (2) identify the "at risk" patient, and (3) refer the intractable chronic pain patient to the appropriate resources. A full assessment of the patient is required to determine the best approach in any given case.

Therapy for chronic pain ranges from single modality approaches for the straightforward patient to comprehensive interdisciplinary care for the more challenging patient. Therapeutic components such as pharmacologic, interventional, psychological and physical have been found to be most effective when performed in an integrated manner. All therapies are focused on the goal of functional restoration rather than merely the elimination of pain and assessment of treatment efficacy is accomplished by reporting functional improvement. Typically, with increased function comes a perceived reduction in pain and increased perception of its control. This ultimately leads to an improvement in the patient's quality of life and a reduction of pain's impact on society.

## References

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**Part 2 – Pain Interventions and Treatments:** All of the following (listed alphabetically) are adapted from ODG except where indicated by “[DWC]”.

## **Acetaminophen**

See Medications for Acute Pain

## **Actiq®**

Not recommended for musculoskeletal pain. Actiq® (oral transmucosal fentanyl citrate), a fast-acting highly addictive "lollipop" painkiller, is indicated only for the management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. See Opioids.

## **Acupuncture [DWC]**

See Section 9792.24.1 of the California Code of Regulations, Title 8, under the Special Topics section. This section addresses the use of acupuncture for chronic pain in the workers' compensation system in California.

## **Anticonvulsants**

See Anti-epilepsy drugs (AEDs)

## **Antidepressants for chronic pain**

Recommended as a first line option for neuropathic pain, and as a possibility for non-neuropathic pain, with duration of about 4-6 weeks required to effectively measure treatment outcome. Have caution regarding sedation with the tricyclics and some other medications due to increased risk of accidents. (Feuerstein, 1997) (Perrot, 2006) Analgesia occurs within a few days and at a lower dose than the antidepressant effect. (Saarto-Cochrane, 2005) Assessment of treatment efficacy should include not only pain outcomes, but also an evaluation of function, changes in use of other analgesic medication, sleep quality and duration, and psychological assessment. (See also Comorbid psychiatric disorders.) It is recommended that these outcome measurements should be initiated at one week of treatment. (Perrot, 2006) (Schnitzer, 2004) (Lin-JAMA, 2003) (Salerno, 2002) (Moulin, 2001) (Fishbain, 2000) (Taylor, 2004) (Gijsman, 2004) (Jick-JAMA, 2004) (Barbui, 2004) (Asnis, 2004) (Stein, 2003) (Pollack, 2003) (Ticknor, 2004) (Staiger, 2003) For more detailed recommendations, see Antidepressants for neuropathic pain and Antidepressants for non-neuropathic pain.

## **Antidepressants for neuropathic pain**

Recommended as a first-line option for neuropathic pain, as indicated below. Tricyclic antidepressants are recommended over selective serotonin reuptake inhibitors (SSRIs), unless adverse reactions are a problem. Caution is required because tricyclics have a low threshold for toxicity, and tricyclic antidepressant overdose is a significant cause of fatal drug poisoning due

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to their cardiovascular and neurological effects. Tricyclic antidepressants have been shown in both a meta-analysis (McQuay, 1996) and a systematic review (Collins, 2000) to be effective, and are considered a first-line treatment. (Namaka, 2004) (Dworkin, 2003) (Gilron, 2006) (Wolfe, 2004) This class of medications works in both patients with normal mood and patients with depressed mood when used in treatment for neuropathic pain. (Sindrup, 2005) Indications in controlled trials have shown effectiveness in treating central post-stroke pain, post-herpetic neuralgia, painful diabetic and non-diabetic polyneuropathy, and post-mastectomy pain. Negative results were found for spinal cord pain and phantom-limb pain, but this may have been due to study design. (Finnerup, 2005) Tricyclics have not been found to be effective for HIV-related neuropathy. A second class of antidepressants documented to be effective in controlled trials include selective serotonin and norepinephrine reuptake inhibitors (SNRIs), with examples being venlafaxine (Effexor®) and duloxetine (Cymbalta®), but there is some controversy regarding the doses of venlafaxine required to inhibit noradrenaline reuptake. (Blier, 2007) This class of medications has been shown to be effective for painful polyneuropathy (both diabetic and non-diabetic). (Sindrup, 2005) Bupropion (Wellbutrin®), a second-generation non-tricyclic antidepressant (a noradrenaline and dopamine reuptake inhibitor) has been shown to be effective in relieving neuropathic pain of different etiologies in a small trial (41 patients). (Finnerup, 2005) While bupropion has shown efficacy in neuropathic pain there is no evidence of efficacy in patients with non-neuropathic chronic low back pain. (Katz, 2005) The use of selective serotonin reuptake inhibitors (SSRIs), a class of antidepressants that inhibit serotonin reuptake without action on noradrenaline, is controversial based on controlled trials. (Finnerup, 2005) (Saarto-Cochrane, 2005) It has been suggested that the main role of SSRIs may be in addressing psychological symptoms associated with chronic pain. (Namaka, 2004) Regardless of the antidepressant chosen, the effect of this class of medication in combination with other medications has not been well researched. (Finnerup, 2005) The “number needed to treat” (NNT) methodology (calculated as the reciprocal value of the response rate on active and placebo) has also been used to calculate efficacy of the different classes of antidepressants. (Sindrup, 2005) Overall, the NNT for amitriptyline (a tricyclic antidepressant) was 2 (1.7 to 2.5). (Saarto-Cochrane, 2005) For peripheral neuropathic pain (excluding HIV) the NNT for tricyclics is 2.3 (2.1-2.7) versus SSRIs of 6.8 (3.4-4.4, studied in painful diabetic polyneuropathy). For the SNRI venlafaxine in painful polyneuropathy using on the dose level of 150 to 250 mg/day), the NNT was 4.6 (2.9-10.6). The NNT for the above trial of 41 patients for Bupropion was 1.3 (1.6-2.1). (Finnerup, 2005) The results of the Saarto-Cochrane study are slightly different than the others mentioned as they grouped SSRIs and SNRIs into one category. Side effects of antidepressants as well as drug-drug interactions play a role in their selection for patients with chronic pain. Tricyclics are contraindicated in patients with cardiac conduction disturbances and/or decompensation as well as those patients with epilepsy. They create anticholinergic side effects of dry mouth, sweating, dizziness, orthostatic hypotension, fatigue, constipation, and problems with micturition. (Finnerup, 2005) To minimize side effects, it is suggested that titration should be slow and based on the patient’s response. (Namaka, 2004) For medications like amitriptyline, the starting dose may be as low as 10-25 mg at night, with increases of 10-25 mg once or twice a week up to 150 mg/day. The Saarto-Cochrane review suggests a trial of SSRIs if a patient is unable to tolerate atypical antidepressants, but it must be remembered that they grouped SSRIs and SNRIs into one category. Using the data presented by Finnerup and Sindrup, a better alternative choice may be a SNRI or Bupropion.

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## Antidepressants for non-neuropathic pain

Recommended as an option in depressed patients with non-neuropathic pain, but effectiveness is limited. Non-neuropathic pain is generally treated with analgesics and anti-inflammatories. There have been 25 controlled trials that have studied the use of antidepressants for fibromyalgia, including 3 meta-analyses. Except for good results found with duloxetine and fibromyalgia (Arnold, 2005), the results generally show limited effectiveness on only a minority of patients for this condition, and most of these studies evaluated tricyclics. (Perrot, 2006) (Moulin, 2001) There appears to be a large placebo effect of this class of medications in treatment of this condition. Four reviews have studied the treatment of low back pain, and tricyclic antidepressants were found to be slightly more effective than placebo for the relief of pain. A non-statistically significant improvement was also noted in improvement of functioning. No studies have specifically studied the use of antidepressants to treat pain from osteoarthritis. (Perrot, 2006) In depressed patients with osteoarthritis, improving depression symptoms was found to decrease pain and improve functional status. (Lin-JAMA, 2003) In guidelines recommended by Perrot it was suggested that antidepressants may be prescribed as analgesics in non-depressed patients, with the first-line choice being tricyclics initiated at a low dose, increasing to a maximally tolerated dose. They also suggested that trials of newer classes of antidepressants should only be initiated if tricyclics proved to be ineffective, if the patient was unable to tolerate side effects, or they were contraindicated.

## Antiepilepsy drugs (AEDs)

*Anti-epilepsy drugs (AEDs) are also referred to as anti-convulsants.*

Recommended for neuropathic pain (pain due to nerve damage), but not for acute somatic pain. (Gilron, 2006) (Wolfe, 2004) (Washington, 2005) (ICSI, 2005) (Wiffen-Cochrane, 2005) (Attal, 2006) (Wiffen-Cochrane, 2007) (Gilron, 2007) (ICSI, 2007) There is a lack of expert consensus on the treatment of neuropathic pain in general due to heterogeneous etiologies, symptoms, physical signs and mechanisms. Most randomized controlled trials (RCTs) for the use of this class of medication for neuropathic pain have been directed at postherpetic neuralgia and painful polyneuropathy (with diabetic polyneuropathy being the most common example). There are few RCTs directed at central pain and none for painful radiculopathy. (Attal, 2006) The choice of specific agents reviewed below will depend on the balance between effectiveness and adverse reactions. See also specific drug listings below: Gabapentin (Neurontin®); Pregabalin (Lyrica®); Lamotrigine (Lamictal®); Carbamazepine (Tegretol®); Oxcarbazepine (Trileptal®); Phenytoin (Dilantin®); Topiramate (Topamax®); Levetiracetam (Keppra®); Zonisamide (Zonegran®); & Tiagabine (Gabitril®)

Outcomes: A “good” response to the use of AEDs has been defined as a 50% reduction in pain and a “moderate” response as a 30% reduction. It has been reported that a 30% reduction in pain is clinically important to patients and a lack of response of this magnitude may be the “trigger” for the following: (1) a switch to a different first-line agent (TCA, SNRI or AED are considered first-line treatment); or (2) combination therapy if treatment with a single drug agent fails. (Eisenberg, 2007) (Jensen, 2006) After initiation of treatment there should be documentation of pain relief and improvement in function as well as documentation of side effects incurred with

## CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

use. The continued use of AEDs depends on improved outcomes versus tolerability of adverse effects. AEDs are associated with teratogenicity, so they must be used with caution in woman of childbearing age.

Specifically studied disease states: (also see below for specific drugs)

Painful polyneuropathy: AEDs are recommended on a trial basis (gabapentin/pregabalin) as a first-line therapy for painful polyneuropathy (with diabetic polyneuropathy being the most common example). The other first-line options are a tri-cyclic antidepressant (if tolerated by the patient), or a SNRI antidepressant (such as duloxetine). (Attal, 2006) (Jensen, 2006)

Postherpetic neuralgia: Gabapentin and pregabalin are recommended. (Attal, 2006) (Backonja, 2004)

Central pain: There are so few trials (with such small sample size) that treatment is generally based on that recommended for peripheral neuropathy, with gabapentin and pregabalin recommended. Lamotrigine has been found to be effective for central post-stroke pain (see below for specific drugs), and gabapentin has also been found to be effective. (Backonja, 2004)

Acute pain: Not indicated due to lack of evidence.

Chronic non-specific axial low back pain: There is no evidence to support the use of these medications for this indication.

Treatment of pain associated with osteoarthritis of the hip: Not indicated

Spinal cord injury: Gabapentin is recommended for chronic neuropathic pain. (Levendoglu, 2004)

CRPS: Gabapentin has been recommended (Serpell, 2002)

Fibromyalgia: Gabapentin and pregabalin have been found to be safe and efficacious to treat pain and other symptoms. (Arnold, 2007) (Crofford, 2005) Pregabalin is FDA approved for fibromyalgia.

Lumbar spinal stenosis: Gabapentin produced statistically significant improvement in walking distance, decrease in pain with movement and sensory deficit in a pilot study. (Yaksi, 2007)

Myofascial pain: Not recommended. There is a lack of evidence to demonstrate that AEDs significantly reduce the level of myofascial or acute musculoskeletal pain, or other sources of somatic pain. (Wiffen-Cochrane, 2005) (Washington, 2005)

Postop pain: AEDs may also be an option for postoperative pain, resulting in decreased opioid consumption. (Peng, 2007) (Buvanendran, 2007)

**SPECIFIC ANTI-EPILEPSY DRUGS:**

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Gabapentin (Neurontin®) has been shown to be effective for treatment of diabetic painful neuropathy and postherpetic neuralgia and has been considered as a first-line treatment for neuropathic pain. (Backonja, 2002) (ICSI, 2007) (Knotkova, 2007) (Eisenberg, 2007) (Attal, 2006) It has been given FDA approval for treatment of post-herpetic neuralgia. The number needed to treat (NNT) for overall neuropathic pain is 4. It has a more favorable side-effect profile than Carbamazepine, with a number needed to harm of 2.5. (Wiffen2-Cochrane, 2005) (Zaremba, 2006) Gabapentin in combination with morphine has been studied for treatment of diabetic neuropathy and postherpetic neuralgia. When used in combination the maximum tolerated dosage of both drugs was lower than when each was used as a single agent and better analgesia occurred at lower doses of each. (Gilron-NEJM, 2005) Recommendations involving combination therapy require further study.

Mechanism of action: This medication appears to be effective in reducing abnormal hypersensitivity (allodynia and hyperalgesia), to have anti-anxiety effects, and may be beneficial as a sleep aid. (Arnold, 2007)

Specific pain states:

Acute pain: There is limited evidence to show that this medication is effective for acute pain, and for postoperative pain, where there is fairly good evidence that the use of gabapentin and gabapentin-like compounds results in decreased opioid consumption. This beneficial effect, which may be related to an anti-anxiety effect, is accompanied by increased sedation and dizziness. (Peng, 2007) (Buvanendran, 2007) (Menigaux, 2005) (Pandey, 2005)

Spinal cord injury: Recommended as a trial for chronic neuropathic pain that is associated with this condition. (Levendoglu, 2004)

CRPS: Recommended as a trial. (Serpell, 2002)

Fibromyalgia: Recommended as a trial. (Arnold, 2007)

Lumbar spinal stenosis: Recommended as a trial, with statistically significant improvement found in walking distance, pain with movement, and sensory deficit found in a pilot study. (Yaksi, 2007)

Side-Effect Profile: Gabapentin has a favorable side-effect profile, few clinically significant drug-drug interactions and is generally well tolerated; however, common side effects include dizziness, somnolence, confusion, ataxia, peripheral edema, and dry mouth. (Eisenberg, 2007) (Attal, 2006) Weight gain is also an adverse effect.

Dosing Information:

Postherpetic neuralgia – Starting regimen of 300 mg once daily on Day 1, then increase to 300 mg twice daily on Day 2; then increase to 300 mg three times daily on Day 3. Dosage may be increased as needed up to a total daily dosage of 1800 mg in three divided doses. Doses above

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1800 mg/day have not demonstrated an additional benefit in clinical studies. (Neurontin package insert)

Diabetic neuropathy (off-label indication) – Gabapentin dosages range from 900 mg to 3600 mg in three divided doses (Backonja, 2002) (Eisenberg, 2007). Gabapentin is 100% renally excreted.

Recommended Trial Period: One recommendation for an adequate trial with gabapentin is three to eight weeks for titration, then one to two weeks at maximum tolerated dosage. (Dworkin, 2003) The patient should be asked at each visit as to whether there has been a change in pain or function. Current consensus based treatment algorithms for diabetic neuropathy suggest that if inadequate control of pain is found, a switch to another first-line drug is recommended. Combination therapy is only recommended if there is no change with first-line therapy, with the recommended change being at least 30%. (TCA, SNRI or AED). (Jensen, 2006) (Eisenberg, 2007)

Weaning and/or changing to another drug in this class: Gabapentin should not be abruptly discontinued, although this recommendation is made based on seizure therapy. Weaning and/or switching to another drug in this class should be done over the minimum of a week. (Neurontin package insert) When to switch to pregabalin: If there is evidence of inadequate response, intolerance, hypersensitivity or contraindications. There have been no head-to-head comparison trails of the two drugs.

Pregabalin (Lyrica®) has been documented to be effective in treatment of diabetic neuropathy and postherpetic neuralgia, has FDA approval for both indications, and is considered first-line treatment for both. This medication is designated as a Schedule V controlled substance because of its causal relationship with euphoria. (Blommel, 2007) This medication also has an anti-anxiety effect. Pregabalin is being considered by the FDA as treatment for generalized anxiety disorder and social anxiety disorder. In June 2007 the FDA announced the approval of pregabalin as the first approved treatment for fibromyalgia. (ICSI, 2007) (Tassone, 2007) (Knotkova, 2007) (Eisenberg, 2007) (Crofford, 2005) Dose adjustment is necessary in patients with renal insufficiency.

Side-Effect Profile: Pregabalin has been associated with many side effects including edema, CNS depression, weight gain, and blurred vision. Somnolence and dizziness have been reported to be the most common side effects related to tolerability. (Tassone, 2007) (Attal, 2006) It has been suggested that this drug be avoided if the patient has a problem with weight gain. (Jensen, 2006)

### Dosing Information:

Diabetic neuropathy – Begin with 50 mg 3 times a day; may be increased in one week based on tolerability and effect to a maximum of 300 mg/day. (Doses up to 600 mg/day were evaluated with no additional benefit and increase in side effects.)

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Postherpetic neuralgia - Begin with 50 mg three times a day for one week; may be increased to 100 mg three times a day after one week based on tolerability and effect. Dose may be increased as tolerated after two to four weeks up to 300 mg twice daily (maximum dose 600 mg/day). (ICSI, 2007)

Trial period: There is no established trial period, but the onset of action is thought to be less than 1 week. (Attal, 2006)

Weaning: Do not discontinue pregabalin abruptly and weaning should occur over a one-week period. Withdrawal effects have been reported after abrupt discontinuation.

Lamotrigine (Lamictal®) has been proven to be moderately effective for treatment of trigeminal neuralgia, HIV, and central post-stroke pain; (Backonja, 2002) (Namaka, 2004) (Maizels, 2005) (ICSI, 2005) (Dworkin, 2003) (Wiffen-Cochrane, 2007). It has not been shown to be effective for diabetic neuropathy. Due to side-effects and slow titration period, lamotrigine is not generally recommended as a first-line treatment for neuropathic pain. (Dworkin, 2003) (ICSI, 2007) Furthermore, a recent Cochrane review determined that although there is some evidence that lamotrigine may be effective for HIV neuropathy and post-stroke pain, this drug does not have a “significant place in therapy at present.” This was partly due to the availability of more effect treatments including other AEDs and antidepressants. (Wiffen-Cochrane, 2007)

Side-Effect Profile: Lamotrigine is associated with many side effects, including a life-threatening skin rash, Stevens-Johnson syndrome (incidence 1/1000), and it has been reported that up to 7% developed a skin rash that may be dose-dependent. (Wiffen-Cochrane, 2007) There is a black box warning regarding skin rashes for this medication. The drug should be discontinued at first sign of rash. (Eisenberg, 2007) Other side effects include dizziness, nausea, headache and fatigue.

Dosing Information: (off-label indication) Begin with 25 mg daily; then titrate up by 25 mg to 50 mg every 1-2 weeks up to 400 mg/day; titration must occur slowly and tapering should occur upon discontinuation. (ICSI, 2007)

Carbamazepine (Tegretol®) has been shown to be effective for trigeminal neuralgia (Backonja, 2002) (ICSI, 2007) (Finnerup, 2005) and has been FDA approved for this indication. The NNT for this medication for trigeminal neuralgia has been reported as 2.6. (Backonja, 2002)

Side Effect Profile: Carbamazepine’s use is often limited because of side-effects, (Knotkova, 2007) including ataxia, cognitive decreases (Namaka, 2004), dizziness, somnolence, CNS depression, hyponatremia, nausea and vomiting, skin rashes (rarely Stevens-Johnson Syndrome has been reported) and hematologic disorders, including agranulocytosis and aplastic anemia. There is a black box warning regarding development of potentially fatal blood cell abnormalities following the use of carbamazepine, and the drug should be discontinued at the first sign of a rash. Pretreatment CBC should be obtained for monitoring purposes; other monitoring parameters include: CBC with platelet count, reticulocytes, serum iron, lipid panel, liver function tests, urinalysis, BUN, serum carbamazepine levels, thyroid function tests, serum sodium; ophthalmic exams (pupillary reflexes). Patient should also be observed for excessive sedation during initial therapy or when increasing dose. Additionally, a long-term effect of weight gain

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has been reported. This medication also has significant drug-drug interactions. The number needed to treat (NNT) for this medication for overall neuropathic pain is 2.5; while the number needed to harm found in the Cochrane review was 3.7. (Wiffen-Cochrane, 2005)

### Dosing Information:

Trigeminal neuralgia – Begin with 100 mg twice daily with food; increase in increments of 100 mg twice daily as needed as tolerated. Usual dose is between 400-800 mg daily in two divided doses. Maximum dose 1200 mg/day.

Oxcarbazepine (Trileptal®) has demonstrated benefits for treating neuropathic pain, specifically trigeminal neuralgia and diabetic neuropathy (ICSI, 2007).

Side-Effect Profile: Similar side-effect profile to carbamazepine (see above). Generally better tolerated when compared to carbamazepine and fewer drug-drug interactions (ICSI, 2007) Serum sodium should be monitored (i.e., especially during initial three-month period).

Dosing Information: Trigeminal neuralgia (off-label indication) - Titrate as tolerated to effect, using recommended dosage titration schedules. Starting doses of 150 mg to 300 mg twice daily; may be titrated by no more than 600 mg/day at weekly intervals to a maximum of 2400 mg daily. Most patients respond to doses between 900 mg—2400 mg/day. (ICSI, 2007) Dose adjustment is necessary in patients with renal insufficiency; use in patients with severe hepatic insufficiency has not been established.

### Other Antiepileptic Drugs

Phenytoin (Dilantin®) has been shown to have limited effectiveness to treat neuropathic pain, except for possible use in acute flares above baseline, and then, given as an IV injection. (Namaka, 2004)

Topiramate (Topamax®) has been shown to have variable efficacy, with failure to demonstrate efficacy in neuropathic pain of “central” etiology. It is still considered for use for neuropathic pain when other anticonvulsants fail. Topiramate has recently been investigated as an adjunct treatment for obesity, but the side effect profile limits its use in this regard. (Rosenstock, 2007)

Levetiracetam (Keppra®), Zonisamide (Zonegran®), and Tiagabine (Gabitril®), are among the antiepileptic drugs (AEDs) most recently approved, while these drugs may be effective for neuropathic pain, the ultimate role of these agents for pain requires further research and experience (ICSI, 2007) (Knotkova, 2007) (Eisenberg, 2007). In the interim, these agents should be used to treat neuropathic pain only when carbamazepine, gabapentin, or lamotrigine cannot be used. (Guay, 2003) In addition, underlying depression and anxiety symptoms may be exacerbated by levetiracetam. (Ettinger, 2007)

### Anti-inflammatory medications

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For specific recommendations, see NSAIDs (non-steroidal anti-inflammatory drugs). Anti-inflammatories are the traditional first line of treatment, to reduce pain so activity and functional restoration can resume, but long-term use may not be warranted. (Van Tulder-Cochrane, 2000) A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain concludes that available evidence supports the effectiveness of non-selective nonsteroidal anti-inflammatory drugs (NSAIDs) in acute and chronic LBP, of muscle relaxants in acute LBP, and of antidepressants in chronic LBP. (Schnitzer, 2004) See also Nonprescription Medications. COX-2 inhibitors (e.g., Celebrex) may be considered if the patient has a risk of GI complications, but not for the majority of patients. Generic NSAIDs and COX-2 inhibitors have similar efficacy and risks when used for less than 3 months, but a 10-to-1 difference in cost. (Rate of overall GI bleeding is 3% with COX-2's versus 4.5% with ibuprofen.) (Homik, 2003) For precautions in specific patient populations, see NSAIDs, GI symptoms & cardiovascular risk.

## **Antispastic agents**

See Muscle relaxants.

## **Baclofen**

See CRPS, sympathetic and epidural blocks. See also Muscle relaxants

## **Barbiturate-containing analgesic agents (BCAs)**

Not recommended for chronic pain. The potential for drug dependence is high and no evidence exists to show a clinically important enhancement of analgesic efficacy of BCAs due to the barbiturate constituents. (McLean, 2000) Fioricet is commonly used for acute headache, with some data to support it, but there is a risk of medication overuse as well as rebound headache. (Friedman, 1987). See also Opioids

## **Behavioral interventions**

Recommended. The identification and reinforcement of coping skills is often more useful in the treatment of pain than ongoing medication or therapy, which could lead to psychological or physical dependence.

## **Benzodiazepines**

Not recommended for long-term use because long-term efficacy is unproven and there is a risk of dependence. Most guidelines limit use to 4 weeks. Their range of action includes sedative/hypnotic, anxiolytic, anticonvulsant, and muscle relaxant. Chronic benzodiazepines are the treatment of choice in very few conditions. Tolerance to hypnotic effects develops rapidly. Tolerance to anxiolytic effects occurs within months and long-term use may actually increase anxiety. A more appropriate treatment for anxiety disorder is an antidepressant. Tolerance to anticonvulsant and muscle relaxant effects occurs within weeks. (Baillargeon, 2003) (Ashton, 2005)

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## Biofeedback

Not recommended as a stand-alone treatment, but recommended as an option in a cognitive behavioral therapy (CBT) program to facilitate exercise therapy and return to activity. There is fairly good evidence that biofeedback helps in back muscle strengthening, but evidence is insufficient to demonstrate the effectiveness of biofeedback for treatment of chronic pain. Biofeedback may be approved if it facilitates entry into a CBT treatment program, where there is strong evidence of success. As with yoga, since outcomes from biofeedback are very dependent on the highly motivated self-disciplined patient, we recommend approval only when requested by such a patient, but not adoption for use by any patient. EMG biofeedback may be used as part of a behavioral treatment program, with the assumption that the ability to reduce muscle tension will be improved through feedback of data regarding degree of muscle tension to the subject. The potential benefits of biofeedback include pain reduction because the patient may gain a feeling that he is in control and pain is a manageable symptom. Biofeedback techniques are likely to use surface EMG feedback so the patient learns to control the degree of muscle contraction. The available evidence does not clearly show whether biofeedback's effects exceed nonspecific placebo effects. It is also unclear whether biofeedback adds to the effectiveness of relaxation training alone. The application of biofeedback to patients with CRPS is not well researched. However, based on CRPS symptomology, temperature or skin conductance feedback modalities may be of particular interest. (Keefe, 1981) (Nouwen, 1983) (Bush, 1985) (Croce, 1986) (Stuckey, 1986) (Asfour, 1990) (Altmaier, 1992) (Flor, 1993) (Newton-John, 1995) (Spence, 1995) (Vlaeyen, 1995) (NIH-JAMA, 1996) (van Tulder, 1997) (Buckelew, 1998) (Hasenbring, 1999) (Dursun, 2001) (van Santen, 2002) (Astin, 2002) (State, 2002) (BlueCross BlueShield, 2004) This recent report on 11 chronic whiplash patients found that, after 4 weeks of myofeedback training, there was a trend for decreased disability in 36% of the patients. The authors recommended a randomized-controlled trial to further explore the effects of myofeedback training. (Voerman, 2006).

Biofeedback therapy guidelines:

Screen for patients with risk factors for delayed recovery, as well as motivation to comply with a treatment regimen that requires self-discipline.

Initial therapy for these “at risk” patients should be physical therapy exercise instruction, using a cognitive motivational approach to PT.

Possibly consider biofeedback referral in conjunction with CBT after 4 weeks:

- Initial trial of 3-4 psychotherapy visits over 2 weeks
- With evidence of objective functional improvement, total of up to 6-10 visits over 5-6 weeks (individual sessions)
- Patients may continue biofeedback exercises at home

## **Boswellia Serrata Resin (Frankincense) [DWC]**

Boswellia Serrata Resin (Frankincense) is not recommended for chronic pain.

## **Botulinum toxin (Botox)**

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Not recommended for chronic pain disorders, but recommended for cervical dystonia. See more details below.

*Not recommended for the following: headache; fibromyositis; chronic low back pain; chronic neck pain; myofascial pain syndrome; & trigger point injections. Several recent studies have found no statistical support for the use of Botulinum toxin A (BTX-A) for any of the following:*

- Myofascial analgesic pain relief as compared to saline. (Qerama, 2006)
- Use as a specific treatment for myofascial cervical pain as compared to saline. (Ojala, 2006) (Ferrante, 2005) (Wheeler, 1998)
- Injection in myofascial trigger points as compared to dry needling or local anesthetic injections. (Kamanli, 2005) (Graboski, 2005).

Recent systematic reviews have stated that current evidence does not support the use of BTX-A trigger point injections for myofascial pain. (Ho, 2006) Or for mechanical neck disease (as compared to saline). (Peloso-Cochrane, 2006) There is one recent study that has found statistical improvement with the use of BTX-A compared to saline. Study patients had at least 10 trigger points and no patient in the study was allowed to take an opioid in the 4 weeks prior to treatment. (Gobel, 2006), And Some additional new data also suggests that it may be effective for low back pain. (Jabbari, 2006) (Ney, 2006)

*Recommended: cervical dystonia*, a condition that is not generally related to workers' compensation injuries (also known as spasmodic torticollis), and is characterized as a movement disorder of the nuchal muscles, characterized by tremor or by tonic posturing of the head in a rotated, twisted, or abnormally flexed or extended position or some combination of these positions. When treated with BTX-B, high antigenicity limits long-term efficacy. Botulinum toxin A injections provide more objective and subjective benefit than trihexyphenidyl or other anticholinergic drugs to patients with cervical dystonia.

### **Bupropion (Wellbutrin®)**

See Antidepressants for Neuropathic pain

### **Cannabinoids**

Not recommended. In total, 11 states have approved the use of medical marijuana for the treatment of chronic pain, but there are no quality controlled clinical data with cannabinoids. Restricted legal access to Schedule I drugs, such as marijuana, tends to hamper research in this area. It is also very hard to do controlled studies with a drug that is psychoactive because it is hard to blind these effects. At this time it is difficult to justify advising patients to smoke street-grade marijuana, presuming that they will experience benefit, when they may also be harmed. (Mackie, 2007) (Moskowitz, 2007)

### **Capsaicin, topical [ODG]**

Recommended only as an option in patients who have not responded or are intolerant to other treatments.

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Formulations: Capsaicin is generally available as a 0.025% formulation (as a treatment for osteoarthritis) and a 0.075% formulation (primarily studied for post-herpetic neuralgia, diabetic neuropathy and post-mastectomy pain). There have been no studies of a 0.0375% formulation of capsaicin and there is no current indication that this increase over a 0.025% formulation would provide any further efficacy.

Indications: There are positive randomized studies with capsaicin cream in patients with osteoarthritis, fibromyalgia, and chronic non-specific back pain, but it should be considered experimental in very high doses. Although topical capsaicin has moderate to poor efficacy, it may be particularly useful (alone or in conjunction with other modalities) in patients whose pain has not been controlled successfully with conventional therapy. The number needed to treat in musculoskeletal conditions was 8.1. The number needed to treat for neuropathic conditions was 5.7. (Mason-BMJ, 2004) (Keitel, 2001) (Robbins, 2000)

Mechanism of action: Capsaicin, which is derived from chili peppers, causes vasodilation, itching, and burning when applied to the skin. These actions are attributed to binding with nociceptors, which causes a period of enhanced sensitivity followed by a refractory period of reduced sensitivity. Topical capsaicin is superior to placebo in relieving chronic neuropathic and musculoskeletal pain. Capsaicin produces highly selective regional anesthesia by causing degeneration of capsaicin-sensitive nociceptive nerve endings, which can produce significant and long lasting increases in nociceptive thresholds. (Maroon, 2006)

Adverse reactions: Local adverse reactions were common (one out of three patients) but seldom serious (burning, stinging, erythema). Coughing has also been reported. . See also CRPS, medications; Diabetic neuropathy; & Topical analgesics.

### **Carbamazepine (Tegretol®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Carbamazepine listing.

### **Carisoprodol (Soma®)**

See Muscle relaxants.

### **Celebrex®**

See Anti-inflammatory medications

### **Chiropractic treatment**

See Manual therapy & manipulation

### **Chondroitin sulfate**

See Glucosamine (and Chondroitin Sulfate).

# CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

## Chronic pain programs

Recommended where there is access to programs with proven successful outcomes, for patients with conditions that put them at risk of delayed recovery. Patients should also be motivated to improve and return to work, and meet the patient selection criteria outlined below. Also called Multidisciplinary pain programs or Interdisciplinary rehabilitation programs, these pain rehabilitation programs combine multiple treatments, and at the least, include psychological care along with physical therapy (including an active exercise component as opposed to passive modalities). While recommended, the research remains ongoing as to (1) what is considered the “gold-standard” content for treatment; (2) the group of patients that benefit most from this treatment; (3) the ideal timing of when to initiate treatment; (4) the intensity necessary for effective treatment; and (5) cost-effectiveness. It has been suggested that interdisciplinary/multidisciplinary care models for treatment of chronic pain may be the most effective way to treat this condition. (Flor, 1992) (Gallagher, 1999) (Guzman, 2001) (Gross, 2005) (Sullivan, 2005) (Dysvik, 2005) (Airaksinen, 2006) (Schonstein, 2003) (Sanders, 2005) (Patrick, 2004) (Buchner, 2006) Unfortunately, being a claimant may be a predictor of poor long-term outcomes. (Robinson, 2004) These treatment modalities are based on the biopsychosocial model, one that views pain and disability in terms of the interaction between physiological, psychological and social factors. (Gatchel, 2005) There appears to be little scientific evidence for the effectiveness of multidisciplinary biopsychosocial rehabilitation compared with other rehabilitation facilities for neck and shoulder pain, as opposed to low back pain and generalized pain syndromes. (Karjalainen, 2003)

Types of programs: There is no one universal definition of what comprises interdisciplinary/multidisciplinary treatment. The most commonly referenced programs have been defined in the following general ways (Stanos, 2006):

(1) Multidisciplinary programs: Involves one or two specialists directing the services of a number of team members, with these specialists often having independent goals. These programs can be further subdivided into four levels of pain programs:

- (a) Multidisciplinary pain centers (generally associated with academic centers and include research as part of their focus)
- (b) Multidisciplinary pain clinics
- (c) Pain clinics
- (d) Modality-oriented clinics

(2) Interdisciplinary pain programs: Involves a team approach that is outcome focused and coordinated and offers goal-oriented interdisciplinary services. Communication on a minimum of a weekly basis is emphasized. The most intensive of these programs is referred to as a Functional Restoration Program, with a major emphasis on maximizing function versus minimizing pain. See Functional restoration programs.

Types of treatment: Components suggested for interdisciplinary care include the following services delivered in an integrated fashion: (a) physical treatment; (b) medical care and supervision; (c) psychological and behavioral care; (d) psychosocial care; (e) vocational rehabilitation and training; and (f) education.

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Predictors of success and failure: As noted, one of the criticisms of interdisciplinary/multidisciplinary rehabilitation programs is the lack of an appropriate screening tool to help to determine who will most benefit from this treatment. Retrospective research has examined decreased rates of completion of functional restoration programs, and there is ongoing research to evaluate screening tools prior to entry. (Gatchel, 2006) The following variables have been found to be negative predictors of efficacy of treatment with the programs as well as negative predictors of completion of the programs: (1) a negative relationship with the employer/supervisor; (2) poor work adjustment and satisfaction; (3) a negative outlook about future employment; (4) high levels of psychosocial distress (higher pretreatment levels of depression, pain and disability); (5) involvement in financial disability disputes; (6) greater rates of smoking; (7) duration of pre-referral disability time; (8) prevalence of opioid use; and (9) pre-treatment levels of pain. (Linton, 2001) (Bendix, 1998) (McGeary, 2006) (McGeary, 2004) (Gatchel, 2005) See also Chronic pain programs, early intervention; Chronic pain programs, intensity; Chronic pain programs, opioids; and Functional restoration programs.

Criteria for the general use of multidisciplinary pain management programs:

Outpatient pain rehabilitation programs may be considered medically necessary when all of the following criteria are met:

(1) An adequate and thorough evaluation has been made, including baseline functional testing so follow-up with the same test can note functional improvement; (2) Previous methods of treating the chronic pain have been unsuccessful; (3) The patient has a significant loss of ability to function independently resulting from the chronic pain; (4) The patient is not a candidate where surgery would clearly be warranted; (5) The patient exhibits motivation to change, and is willing to forgo secondary gains, including disability payments to effect this change; & (6) Negative predictors of success above have been addressed.

Integrative summary reports that include treatment goals, progress assessment and stage of treatment, must be made available upon request and at least on a bi-weekly basis during the course of the treatment program. Treatment is not suggested for longer than 2 weeks without evidence of demonstrated efficacy as documented by subjective and objective gains.

Inpatient pain rehabilitation programs: These programs typically consist of more intensive functional rehabilitation and medical care than their outpatient counterparts. They may be appropriate for patients who: (1) don't have the minimal functional capacity to participate effectively in an outpatient program; (2) have medical conditions that require more intensive oversight; (3) are receiving large amounts of medications necessitating medication weaning or detoxification; or (4) have complex medical or psychological diagnosis that benefit from more intensive observation and/or additional consultation during the rehabilitation process. (Keel, 1998) (Kool, 2005) (Buchner, 2006) (Kool, 2007) As with outpatient pain rehabilitation programs, the most effective programs combine intensive, daily biopsychosocial rehabilitation with a functional restoration approach.

(BlueCross BlueShield, 2004) (Aetna, 2006) See Functional restoration programs

### **Clonidine, Intrathecal [DWC]**

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Recommended. The evidence supports the use of intrathecal clonidine alone or in conjunction with opioids (e.g., morphine) and local anesthetics (e.g., bupivacaine) in the treatment of Complex Regional Pain Syndrome/Reflex Sympathetic Dystrophy (CRPS/RSD). Intrathecal clonidine can also be used in conjunction with opioids for neuropathic pain. There is no evidence that intrathecal clonidine alone is effective in the treatment of pain after spinal cord surgery. There are no studies that address the use of intrathecal clonidine beyond 18 months.

## **Cod liver oil [DWC]**

Cod liver oil is not recommended for chronic pain.

## **Cognitive behavioral therapy**

See Psychological treatment. See also Multi-disciplinary pain programs

## **Cold lasers**

See Low level laser therapy (LLLT).

## **Complex Regional Pain Syndrome (CRPS)**

### **CRPS, medications**

Recommended only as indicated below. Most medications have limited effectiveness. (Ribbers, 2003) ([Quisel2, 2005](#))

1. Regional inflammatory reaction: Commonly used drugs are NSAIDs, corticosteroids and free-radical scavengers. There is some evidence of efficacy and little likelihood for harm for topical DMSO cream, IV bisphosphonates and limited courses of oral corticosteroids. Corticosteroids are most effective when positive response is obtained with sympathetic blocks. NSAIDs are recommended but no trials have shown effectiveness in CRPS-I, and they are recommended primarily in early or very late stages. (Stanton-Hicks, 2004) (Sharma, 2006)

2. Stimulus-independent pain: The use of antidepressants, anticonvulsants, and opioids has been primarily extrapolated based on use for other neuropathic pain disorders. (See Antidepressants for neuropathic pain; Anticonvulsants for chronic pain; & Opioids for neuropathic pain.) Mexiletine (oral lidocaine), lidocaine patches and capsaicin are used but efficacy is not convincing. For central inhibition opiates, gabapentin, TCAs, GABA-enhancing drugs, and clonidine may be useful.

3. Stimulus-evoked pain: treatment is aimed at central sensitization. With NMDA receptor antagonists (ketamine and amantadine) convincing controlled trials are lacking, and these drugs are known for their side effects.

## CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

4. Sympathetically maintained pain (SMP):  $\alpha$ 1 adrenoceptor blocking agents (terazosin, prazosin, and phenoxybenzamine) have been shown to be effective in a case report. (Ghostine, 1984) Sympathetic suppressors such as guanethadine, reserpine, droperidol, or atropine (in general or IV block) have shown low effectiveness. (Perez, 2001) (Quisel2, 2005) Phentolamine (IV) has been used as an alternative to determine responsiveness to  $\alpha$ 1 adrenoceptor blocking agents. See also Sympathetically maintained pain (SMP).

5. Treatment of bone resorption with bisphosphonate-type compounds and calcitonin. Significant improvement has been found in limited studies of intravenous clodronate and intravenous alendronate. Adendronate given in oral doses of 40 mg a day (over an 8 week period) produced improvements in pain, pressure tolerance and joint mobility. (Manicourt DH, 2004) Mixed results have been found with intranasal calcitonin. (Sahin, 2005) (Appelboom, 2002) (Rowbathan, 2006) (Sharma, 2006)

### **CRPS, prevention**

Recommended as indicated below. Some cases of CRPS-I may be preventable. Post-stroke upper extremity hemiplegia (also known as shoulder-hand syndrome) may be prevented by early inpatient rehabilitation and avoidance of shoulder trauma to the affected arm. Post-fracture CRPS-I may be prevented with 500 mg vitamin C daily started upon diagnosis of fracture and continued through healing. (Quisel2, 2005)

### **CRPS, spinal cord stimulators (SCS)**

Recommended as indicated below. Spinal cord stimulators (SCS) should be offered only after careful counseling and patient identification and should be used in conjunction with comprehensive multidisciplinary medical management. CRPS patients implanted with SCS reported pain relief of at least 50% over a median follow-up period of 33 months. SCS use has been associated with pain reduction in studies of patients with with CRPS. Moreover, there is evidence to demonstrate that SCS is a cost-effective treatment for CRPS-I over the long term. (Taylor, 2006) (Stanton-Hicks, 2006) (Mailis-Gagnon-Cochrane, 2004) (Kemler, 2000) Permanent pain relief in CRPS-I can be attained under long-term SCS therapy combined with physical therapy. (Harke, 2005) See Spinal cord stimulators (SCS).

### **CRPS, sympathectomy**

Not recommended. The practice of surgical and chemical sympathectomy is based on poor quality evidence, uncontrolled studies and personal experience. Furthermore, complications of the procedure may be significant, in terms of both worsening the pain or producing a new pain syndrome; and abnormal forms of sweating (compensatory hyperhidrosis and pathological gustatory sweating). Therefore, more clinical trials of sympathectomy are required to establish the overall effectiveness and potential risks of this procedure. (Furlan, 2000) (Mailis-Cochrane, 2003) Sympathectomy is destruction of part of the sympathetic nervous system, and it is not generally accepted or widely used. Long-term success with this pain relief treatment is poor. Indications: Single extremity CRPS-I or SMP; distal pain only (should not be done if the proximal extremity is involved). Local anesthetic Stellate Ganglion Block or Lumbar

## CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

Sympathetic Block consistently gives 90 to 100 percent relief each time a technically good block is performed (with measured rise in temperature). The procedure may be considered for individuals who have limited duration of relief from blocks. Permanent neurological complications are common. (State, 2002)

### **CRPS, sympathetic and epidural blocks**

Recommended when used for symptom relief and to demonstrate sympathetically maintained pain (SMP). (Stanton-Hicks, 2004) A systematic review revealed a paucity of published evidence supporting the use of local anesthetic sympathetic blocks for the treatment of CRPS. (Cepeda, 2005) Regional sympathetic blocks are used for (1) Upper extremity: Stellate ganglion blocks or laparoscopic blocks; or (2) Lower extremity: Lumbar sympathetic block. Signs of a successful block: Temperature rise to 35°; Sympathetic skin response using modified ECG; Cold pressor test; Laser Doppler flowmetry. This type of evaluation is important, especially if the block is unsuccessful in eliminating pain in order to determine if a complete block was performed. A sensory examination should also be completed in patients with pain relief. Local anesthetic can also result in somatic block that can affect pain. Pain relief may also be due to systemic uptake of local anesthetic or a placebo effect. (Grabow, 2005) Evaluating and treating results should include: (1) Complete elimination of pain: consider prolonged neurolytic block; consider the use of a  $\alpha_1$  adrenoceptor blocker such as terazosin; & (2) Current suggested guidelines suggest that a maximum sustained benefit is obtained after 3 to 6 blocks when used in addition to PT. (Washington, 2002) (Stanton-Hicks, 2006) They also state that even if the original site is unresponsive, future exacerbations of CRPS at the same site or distant site may respond to 1 to 3 blocks. (Washington, 2002) Alternatives to regional sympathetic blocks may be necessary when there is evidence of coagulopathy, systemic infection, and/or post-surgical changes. These include peripheral nerve and plexus blocks and epidural administration of local anesthetics. Mixed conduction blocks (central neural blocks) are suggested when analgesia is insufficient by pharmacologic means to support physical therapy: (1) Implanted catheters at the brachial or lumbosacral plexus: allows for 1 to 2 weeks of therapy. Side effects include technical failure and infection; & (2) Epidural tunneled catheters: allows for long-term therapy: Side effects: same as above. Clonidine has also been effective epidurally. (Stanton-Hicks, 2006) Baclofen has been demonstrated to be effective intrathecally to reduce dystonia. (van Hilten, 2000) IV regional sympathetic blocks are controversial due to varying success. Guanethidine was used, but is no longer available in the US. Bretylium and reserpine require daily blocks, and have potential side effects of transient syncope with apnea, orthostatic hypotension, pain with administration, nausea and vomiting. Bretylium provided a 30% improvement in pain compared to placebo. Due to modest benefits and the invasiveness of the therapies, epidural clonidine injection and intravenous regional sympathetic block with bretylium should be offered only after careful counseling, and they should be followed by intensive physical therapy. Intravenous regional sympathetic block (Bier's block, 25 sessions) with guanethidine and lidocaine resulted in excellent pain relief and full restoration of both function and range of movement of the affected extremity in patients suffering from CRPS-I of the hand. (Paraskevas, 2005) Local or systemic parecoxib combined with lidocaine/clonidine IV regional analgesia is an effective treatment for CRPS-I in a dominant upper limb. (Frade, 2005) See also Sympathetically maintained pain (SMP).

# CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

## CRPS, treatment

Recommended hierarchy of options as indicated below. The goal is to improve function. Multiple pathophysiological mechanisms are responsible including neuropathic (sympathetic and independently-maintained pain), and immunologic (regional inflammation and altered human leukocyte antigens). Both peripheral sensitization and central sensitization have been proposed. (Ribbers, 2003) (Stanton-Hicks, 2006) There are no evidence-based treatment guidelines but several groups have begun to organize treatment algorithms. Recommendations:

1. Rehabilitation: (a) Early stages: Build a therapeutic alliance. Analgesia, encouragement and education are key. Physical modalities include desensitization, isometric exercises, resisted range of motion, and stress loading. If not applied appropriately, PT can actually be detrimental. (b) Next steps: Increase flexibility with introduction of gentle active ROM and stretching (to treat accompanying myofascial pain syndrome). Other modalities may include muscle relaxants, trigger point injections and electrical stimulation (based on anecdotal evidence). Edema control may also be required (elevation, retrograde sympathetic blocks, diuretics and adrenoceptor blockers when sympathetically maintained pain-SMP is present). (c) Continued steps: Continue active ROM; stress loading; scrubbing techniques; isotonic strengthening; general aerobic conditioning; and postural normalization. (d) Final steps: Normalization of use; assessment of ergonomics, posture and modifications at home and work. In some cases increased requirements of analgesic medications, psychotherapy, invasive anesthetic techniques and SCS may be required. See CRPS, spinal cord stimulators.

2. Psychological treatment: Focused on improved quality of life, development of pain coping skills, cognitive-behavioral therapy, and improving facilitation of other modalities. (a) Early stages: education. (b) Next steps: clinical psychological assessment (after 6 to 8 weeks): identification of stressors; identification of comorbid Axis I psychiatric disorders (depression, anxiety, panic and post-traumatic stress).

3. Pain management: (a) Pharmacological: antidepressants (particularly amitriptyline); anticonvulsants (particularly gabapentin); steroids; NSAIDs; opioids; calcitonin;  $\alpha 1$  adrenoceptor antagonists (terazosin or phenoxybenzamine). The latter class of drugs has been helpful in SMP. Clonidine has been given transdermally and epidurally. (See CRPS, medications.) (b) Minimally invasive: depends on degree of SMP, stage of rehabilitation (passive or active movement), and response to blocks. (See CRPS, sympathetic blocks.) Responders to sympathetic blocks (3 to 6 blocks with concomitant PT) may be all that is required. For non-responders somatic block or epidural infusion may be required to optimize analgesia for PT. (c) More invasive: After failure of progression or partial relief, consider tunneled epidural catheters for prolonged sympathetic or somatic blocks or neurostimulation with SCS in CRPS-I and II. See CRPS, spinal cord stimulators. Also consider peripheral nerve stimulation in CRPS-II and intrathecal drug delivery in patients with dystonia, failed neurostimulation, long-standing disease, multi-limb involvement and requirement of palliative care. (d) Surgical: Sympathectomy is not generally recommended, but has been considered in patients that respond to sympathetic blocks. Pre-procedure the patient should have outcomes assessed with radiofrequency and neurolytic procedures. (See CRPS, sympathectomy.) Motor Cortex Stimulation has been considered.

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Outcome measures for all treatments of CRPS: Objective measures such as the McGill Pain Questionnaire-Short Form, the Pain Disability Index, the Beck Depression Inventory, Treatment Outcomes in Pain Survey, and the State Trait Anxiety Inventory. See Psychological evaluations. See also CRPS, diagnostic criteria; CRPS, medications; CRPS, prevention; CRPS, sympathetic blocks; & Sympathetically maintained pain (SMP). See also Spinal cord stimulators (SCS).

## **CRPS [DWC]**

See Complex Regional Pain Syndrome (CRPS) [DWC]

## **Curcumin (tumeric) [DWC]**

Curcumin (tumeric) is not recommended for the treatment of chronic pain.

## **Cyclobenzaprine (Flexeril®)**

Recommended as an option, using a short course of therapy. See Medications for subacute & chronic pain for other preferred options. Cyclobenzaprine (Flexeril®) is more effective than placebo in the management of back pain; the effect is modest and comes at the price of greater adverse effects. The effect is greatest in the first 4 days of treatment, suggesting that shorter courses may be better. (Browning, 2001) Cyclobenzaprine-treated patients with fibromyalgia were 3 times as likely to report overall improvement and to report moderate reductions in individual symptoms, particularly sleep. (Tofferi, 2004) Note: Cyclobenzaprine is closely related to the tricyclic antidepressants, e.g., amitriptyline. See Antidepressants. Cyclobenzaprine is associated with a number needed to treat of 3 at 2 weeks for symptom improvement in LBP and is associated with drowsiness and dizziness. (Kinkade, 2007)

## **Cymbalta**

See Duloxetine.

## **Cytokine DNA Testing for Pain [DWC]**

Not recommended. There is no current evidence to support the use of cytokine DNA testing for the diagnosis of pain, including chronic pain. Scientific research on cytokines is rapidly evolving.

## **Detoxification**

Recommended as indicated below. Detoxification is defined as withdrawing a person from a specific psychoactive substance, and it does not imply a diagnosis of addiction, abuse or misuse. May be necessary due to the following: (1) Intolerable side effects, (2) Lack of response, (3) Aberrant drug behaviors as related to abuse and dependence, (4) refractory comorbid psychiatric illness, or (5) Lack of functional improvement. Gradual weaning is recommended for long-term

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opioid users because opioids cannot be abruptly discontinued without probable risk of withdrawal symptoms. (Benzon, 2005) See also Rapid detox.

## Drug testing

Recommended as an option, using a urine drug screen to assess for the use or the presence of illegal drugs. For more information, see Opioids, criteria for use: (2) Steps to Take Before a Therapeutic Trial of Opioids & (4) On-Going Management; Opioids, differentiation: dependence & addiction; Opioids, screening for risk of addiction (tests); & Opioids, steps to avoid misuse/addiction.

## Drug therapy

See Medications.

## Duloxetine (Cymbalta®)

Recommended as a first-line treatment option in neuropathic pain. Duloxetine (Cymbalta®) is a norepinephrine and serotonin reuptake inhibitor antidepressant. It has FDA approval for treatment of depression, generalized anxiety disorder, and for the treatment of pain related to diabetic neuropathy, with effect found to be significant by the end of week 1 (effect measured as a 30% reduction in baseline pain). The starting dose is 20-60 mg/day, and no advantage has been found by increasing the dose to twice a day, except in fibromyalgia. The medication has been found to be effective for treating fibromyalgia in women with and without depression, 60 mg once or twice daily. (Arnold, 2005) The most frequent side effects include nausea, dizziness and fatigue. GI symptoms are more common early in treatment. The side effect profile of Duloxetine is thought to be less bothersome to patients than that of tricyclic antidepressants. Note: On October 17, 2005, Eli Lilly and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revision to the PRECAUTIONS/Hepatotoxicity section of the prescribing information for Cymbalta. Postmarketing reports of hepatic injury (including hepatitis and cholestatic jaundice) suggest that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. The new labeling extends the Precaution against using Cymbalta in patients with substantial alcohol use to include those patients with chronic liver disease. It is recommended that Cymbalta not be administered to patients with hepatic insufficiency. See also Antidepressants for neuropathic pain.

## Dynatron STS [DWC]

See Transcutaneous Electrotherapy [DWC]

## Education

Recommended. Education of the patient and family, as well as the employer, insurer, policy makers and the community should be the primary emphasis in the treatment of chronic pain. Currently, practitioners often think of education last, after medications, manual therapy and surgery. Practitioners must develop and implement an effective strategy and skills to educate

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patients, employers, insurance systems, policy makers and the community as a whole. An education-based paradigm should always start with inexpensive communication providing reassuring information to the patient. More in-depth education currently exists within a treatment regime employing functional restorative and innovative programs of prevention and rehabilitation. No treatment plan is complete without addressing issues of individual and/or group patient education as a means of facilitating self-management of symptoms and prevention. (Colorado, 2002)

## **Effexor®**

See Venlafaxine

## **Electrical stimulators (E-stim) [DWC]**

See specific individual treatment topics for treatment guidelines regarding the exact type of electrical stimulation treatment. The following are the choices:

- **See Transcutaneous Electrotherapy [DWC] for**
  - **TENS, chronic pain (transcutaneous electrical nerve stimulation)**
  - **TENS, post operative pain (transcutaneous electrical nerve stimulation)**
  - **Electroceutical therapy (bioelectric nerve block)**
  - **Galvanic stimulation**
  - **Neuromuscular electrical stimulation (NMES)**
  - **H-wave stimulation (devices)**
  - **Interferential current stimulation (ICS)**
  - **Microcurrent electrical stimulation (MENS devices)**
  - **RS-4i sequential stimulator**
  - **Sympathetic therapy**
  - **Dynatron STS**
- **Percutaneous electrical nerve stimulation (PENS)**
- **Percutaneous neuromodulation therapy (PNT)**
- **Spinal cord stimulation**

## **Electroceutical Therapy (bioelectric nerve block) [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **Epidural steroid injections (ESIs)**

Recommended as an option for treatment of radicular pain (defined as pain in dermatomal distribution with corroborative findings of radiculopathy). See specific criteria for use below. Most current guidelines recommend no more than 2 ESI injections. This is in contradiction to previous generally cited recommendations for a “series of three” ESIs. These early recommendations were primarily based on anecdotal evidence. Research has now shown that, on average, less than two injections are required for a successful ESI outcome. Current recommendations suggest a second epidural injection if partial success is produced with the first

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injection, and a third ESI is rarely recommended. Epidural steroid injection can offer short term pain relief and use should be in conjunction with other rehab efforts, including continuing a home exercise program. There is little information on improved function. The American Academy of Neurology recently concluded that epidural steroid injections may lead to an improvement in radicular lumbosacral pain between 2 and 6 weeks following the injection, but they do not affect impairment of function or the need for surgery and do not provide long-term pain relief beyond 3 months, and there is insufficient evidence to make any recommendation for the use of epidural steroid injections to treat radicular cervical pain. (Armon, 2007) See also Epidural steroid injections, “series of three”.

Criteria for the use of Epidural steroid injections:

Note: The purpose of ESI is to reduce pain and inflammation, restoring range of motion and thereby facilitating progress in more active treatment programs, and avoiding surgery, but this treatment alone offers no significant long-term functional benefit.

- 1) Radiculopathy must be documented by physical examination and corroborated by imaging studies and/or electrodiagnostic testing.
- 2) Initially unresponsive to conservative treatment (exercises, physical methods, NSAIDs and muscle relaxants).
- 3) Injections should be performed using fluoroscopy (live x-ray) for guidance.
- 4) If used for diagnostic purposes, a maximum of two injections should be performed. A second block is not recommended if there is inadequate response to the first block. Diagnostic blocks should be at an interval of at least one to two weeks between injections.
- 5) No more than two nerve root levels should be injected using transforaminal blocks.
- 6) No more than one interlaminar level should be injected at one session.
- 7) In the therapeutic phase, repeat blocks should only be offered if there is at least 50% pain relief for six to eight weeks, with a general recommendation of no more than 4 blocks per region per year. (Manchikanti, 2003) (CMS, 2004) (Boswell, 2007)
- 8) Repeat injections should be based on continued objective documented pain and function response.
- 9) Current research does not support a “series-of-three” injections in either the diagnostic or therapeutic phase. We recommend no more than 2 ESI injections.

### Exercise

Recommended. There is strong evidence that exercise programs, including aerobic conditioning and strengthening, are superior to treatment programs that do not include exercise. There is no sufficient evidence to support the recommendation of any particular exercise regimen over any other exercise regimen. A therapeutic exercise program should be initiated at the start of any treatment rehabilitation. Such programs should emphasize education, independence, and the importance of an on-going exercise regime. (State, 2002) (Airaksinen, 2006) A recent study of the long term impact of aerobic exercise on musculoskeletal pain, in a prospective cohort of 866 healthy seniors followed for 14 years, found that exercise was associated with a substantial and significant reduction in pain even after adjusting for gender, baseline BMI and attrition, and despite the fact that fractures, a significant predictor of pain, were slightly more common among exercisers. (Bruce, 2005) A recent trial concluded that active physical treatment, cognitive-behavioral treatment, and the two combined each resulted in equally significant improvement,

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much better compared to no treatment. (The cognitive treatment focused on encouraging increased physical activity.) (Smeets, 2006)

## **Fioricet**

See Barbiturate-containing analgesic agents (BCAs).

## **Fish oil**

See Cod liver oil.

## **Flexeril® (Cyclobenzaprine)**

See Cyclobenzaprine (Flexeril)

## **fMRI (functional magnetic resonance imaging)**

See Functional imaging of brain responses to pain.

## **Functional imaging of brain responses to pain [DWC]**

Not recommended. Functional neuroimaging is helping to identify the sensory and emotional components of pain and its autonomic responses, and may help in the design of more rational treatments for pain. However, this test is only useful in a research setting at this time and does not have a role in the evaluation or treatment of patients.

## **Functional restoration programs (FRPs)**

Recommended, although research is still ongoing as to how to most appropriately screen for inclusion in these programs. Functional restoration programs (FRPs), a type of treatment included in the category of interdisciplinary pain programs (see Chronic pain programs), were originally developed by Mayer and Gatchel. FRPs were designed to use a medically directed, interdisciplinary pain management approach geared specifically to patients with chronic disabling occupational musculoskeletal disorders. These programs emphasize the importance of function over the elimination of pain. FRPs incorporate components of exercise progression with disability management and psychosocial intervention. Long-term evidence suggests that the benefit of these programs diminishes over time, but still remains positive when compared to cohorts that did not receive an intensive program. (Bendix, 1998) A Cochrane review suggests that there is strong evidence that intensive multidisciplinary rehabilitation with functional restoration reduces pain and improves function of patients with low back pain. The evidence is contradictory when evaluating the programs in terms of vocational outcomes. (Guzman 2001) It must be noted that all studies used for the Cochrane review excluded individuals with extensive radiculopathy, and several of the studies excluded patients who were receiving a pension, limiting the generalizability of the above results. Studies published after the Cochrane review also indicate that intensive programs show greater effectiveness, in particular in terms of return to work, than less intensive treatment. (Airaksinen, 2006) There appears to be little scientific

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evidence for the effectiveness of multidisciplinary biopsychosocial rehabilitation compared with other rehabilitation facilities for neck and shoulder pain, as opposed to low back pain and generalized pain syndromes. (Karjalainen, 2003) Treatment is not suggested for longer than 2 weeks without evidence of demonstrated efficacy as documented by subjective and objective gains. For general information see Chronic pain programs.

## **Gabapentin (Neurontin®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Gabapentin listing.

## **Galvanic Stimulation**

Not recommended. Considered investigational for all indications. Galvanic stimulation is characterized by high voltage, pulsed stimulation and is used primarily for local edema reduction through muscle pumping and polarity effect. Edema is comprised of negatively charged plasma proteins, which leak into the interstitial space. The theory of galvanic stimulation is that by placing a negative electrode over the edematous site and a positive electrode at a distant site, the monophasic high voltage stimulus applies an electrical potential which disperses the negatively charged proteins away from the edematous site, thereby helping to reduce edema. (BlueCrossBlueShield, 2005)

## **Glucosamine (and Chondroitin Sulfate) [DWC]**

Glucosamine (and Chondroitin Sulfate) is not recommended for chronic pain.

## **Green tea [DWC]**

Green Tea is not recommended for chronic pain.

## **Herbal medicines [DWC]**

See specific Sections on Boswellia Serrata Resin (Frankincense), Cannabinoids, Curcumin (tumeric), Green Tea, Pycnogenol (maritime pine bark), Uncaria Tomentosa (Cat's Claw), White willow bark

## **Home health services**

Recommended only for otherwise recommended medical treatment for patients who are homebound, on a part-time or “intermittent” basis. Medical treatment does not include homemaker services like shopping, cleaning, and laundry, and personal care given by home health aides like bathing, dressing, and using the bathroom when this is the only care needed. (CMS, 2004)

## **H-Wave stimulation (devices) [DWC]**

See Transcutaneous Electrotherapy [DWC]

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## Hydrocodone (Vicodin®, Lortab®)

See Opioids

## Ibuprofen

See Anti-inflammatory medications.

## Imaging

See Functional imaging of brain responses to pain.

## Implantable drug-delivery systems (IDDSs)

Recommended only as an end-stage treatment alternative for selected patients for specific conditions indicated below, after failure of at least 6 months of less invasive methods, and following a successful temporary trial. Results of studies of opioids for musculoskeletal conditions (as opposed to cancer pain) generally recommend short use of opioids for severe cases, not to exceed 2 weeks, and do not support chronic use (for which a pump would be used), although IDDSs may be appropriate in selected cases of chronic, severe low back pain or failed back syndrome. This treatment should only be used relatively late in the treatment continuum, when there is little hope for effective management of chronic intractable pain from other therapies. (Angel, 1998) (Kumar, 2002) (Hassenbusch, 2004) (Boswell, 2005) For most patients, it should be used as part of a program to facilitate restoration of function and return to activity, and not just for pain reduction. The specific criteria in these cases include the failure of at least 6 months of other conservative treatment modalities, intractable pain secondary to a disease state with objective documentation of pathology, further surgical intervention is not indicated, psychological evaluation unequivocally states that the pain is not psychological in origin, and a temporary trial has been successful prior to permanent implantation as defined by a 50% reduction in pain. (Tutak, 1996) (Yoshida, 1996) (BlueCross, 2005) (United Health Care, 2005) See also Opioids and the Low Back Chapter. In a study of IDDS in 136 patients with low back pain, after one year 87% of the patients described their quality of life as fair to excellent, and 87% said they would repeat the implant procedure. However, complication rates (i.e., infection, dislodging, and cerebrospinal fluid leak) are likely to rise with time in these procedures and more longitudinal outcome studies need to be conducted. (Deer, 2004) In one survey involving 429 patients with nonmalignant pain treated with intrathecal therapy, physician reports of global pain relief scores were excellent in 52.4% of patients, good in 42.9%, and poor in 4.8%. In another study of 120 patients, the mean pain intensity score had fallen from 93.6 to 30.5 six months after initiation of therapy. In both studies, patients reported significant improvement in activities of daily living, quality of life measures, and satisfaction with the therapy. Constipation, urinary retention, nausea, vomiting, and pruritus are typical early adverse effects of intrathecal morphine and are readily managed symptomatically. Other potential adverse effects include amenorrhea, loss of libido, edema, respiratory depression, and technical issues with the intrathecal system. (Winkelmuller, 1996) (Paice, 1997) One study in patients suffering from chronic low back pain caused by failed back syndrome found a 27% improvement after 5 years for patients in the intrathecal drug therapy group, compared with a 12% improvement in the

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control group. (Kumar, 2002) Supporting empirical evidence is significantly supplemented and enhanced when combined with the individually based observational evidence gained through an individual trial prior to implant. This individually based observational evidence should be used to demonstrate effectiveness and to determine appropriate subsequent treatment. Generally, use of implantable pumps is FDA approved and indicated for chronic intractable pain. Treatment conditions may include FBSS, CRPS, Arachnoiditis, Diffuse Cancer Pain, Osteoporosis, and Axial Somatic Pain. As we have gained more experience with this therapy, it has become apparent that even intrathecal opiates, when administered in the long term, can be associated with problems such as tolerance, hyperalgesia, and other side effects. Consequently, long-term efficacy has not been convincingly proven. However, it is important to note that there is a distinction between "tolerance" and "addiction", and the levels of drugs administered intrathecally should be significantly below what might be needed orally in their absence. (Osenbach, 2001) (BlueCross BlueShield, 2005)

Indications for Implantable drug-delivery systems:

Implantable infusion pumps are considered medically necessary when used to deliver drugs for the treatment of:

- o Primary liver cancer (intrahepatic artery injection of chemotherapeutic agents);
- o Metastatic colorectal cancer where metastases are limited to the liver (intrahepatic artery injection of chemotherapeutic agents);
- o Head/neck cancers (intra-arterial injection of chemotherapeutic agents);
- o Severe, refractory spasticity of cerebral or spinal cord origin in patients who are unresponsive to or cannot tolerate oral baclofen (Lioresal®) therapy (intrathecal injection of baclofen)

Permanently implanted intrathecal (intraspinal) infusion pumps for the administration of opiates or non-opiate analgesics, in the treatment of chronic intractable pain, are considered medically necessary when:

- Used for the treatment of malignant (cancerous) pain and all of the following criteria are met:

1. Strong opioids or other analgesics in adequate doses, with fixed schedule (not PRN) dosing, have failed to relieve pain or intolerable side effects to systemic opioids or other analgesics have developed; and

2. Life expectancy is greater than 3 months (less invasive techniques such as external infusion pumps provide comparable pain relief in the short term and are consistent with standard of care); and

3. Tumor encroachment on the thecal sac has been ruled out by appropriate testing; and

4. No contraindications to implantation exist such as sepsis or coagulopathy; and

5. A temporary trial of spinal (epidural or intrathecal) opiates has been successful prior to permanent implantation as defined by a 50% reduction in pain. A temporary trial of intrathecal (intraspinal) infusion pumps is considered medically necessary only when criteria 1-4 above are met.

- Used for the treatment of non-malignant (non-cancerous) pain with a duration of greater than 6 months and all of the following criteria are met:

1. Documentation, in the medical record, of the failure of 6 months of other conservative treatment modalities (pharmacologic, surgical, psychologic or physical), if appropriate and not contraindicated; and

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2. Intractable pain secondary to a disease state with objective documentation of pathology in the medical record; and
3. Further surgical intervention is not indicated; and
4. Psychological evaluation has been obtained and evaluation states that the pain is not primarily psychologic in origin and that benefit would occur with implantation despite any psychiatric comorbidity; and
5. No contraindications to implantation exist such as sepsis or coagulopathy; and
6. A temporary trial of spinal (epidural or intrathecal) opiates has been successful prior to permanent implantation as defined by at least a 50% to 70% reduction in pain and documentation in the medical record of improved function and associated reduction in oral pain medication use. A temporary trial of intrathecal (intraspinal) infusion pumps is considered medically necessary only when criteria 1-5 above are met.

## **Implantable spinal cord stimulators**

See Spinal Cord Stimulators (SCS)

## **Injection with anaesthetics and/or steroids [DWC]**

See Epidural steroid injections (ESI's), Lumbar sympathetic block, Trigger point injections, Stellate ganglion block, and Prolotherapy.

## **Interdisciplinary rehabilitation programs**

See Chronic Pain Programs

## **Interferential Current Stimulation [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **Intrathecal drug delivery systems (IDDSs)**

See Implantable drug-delivery systems (IDDSs).

## **Intrathecal drug delivery systems, medications**

Recommended as indicated below. (The following recommendations were made prior to FDA approval of ziconotide.) (Hassenbusch, 2004)

Recommended 1st stage: Morphine is generally the initial IDDS medication. The maximum recommended dose for this drug is 15 mg/day with a concentration of 30 mg/mL. An alternative non-FDA approved medication is hydromorphone. The maximum recommended dose for this medication is 10 mg/day with a concentration of 30 mg/mL. Other opioids (including Fentanyl and Sufentanil) have been used for intrathecal chronic non-malignant pain but are non-FDA approved and have little research associated with their use. (Waara-Wolleat, 2006)

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Recommended 2nd stage: If side effects occur, an upper limit of dosing is reached, or neuropathic pain is present, clonidine is next recommended as an addition to an opioid (maximum recommended dose of 1 mg/day and a concentration of 2 mg/mL). Bupivacaine has also been recommended as an alternative to clonidine (maximum dose of 30 mg/day and a concentration of 38 mg/mL). Clonidine, which is FDA approved for intrathecal delivery, is thought to provide analgesic effect via a non-opioid mechanism. It has been found to offer only short-term relief when used as a single agent.

Recommended 3rd stage: The recommendation has been made to add both clonidine and bupivacaine. Baclofen has been used to treat intractable spasticity from brain injury, cerebral palsy, and spinal cord injury and has resulted in improvement in muscle tone and pain relief. (Guillaume, 2005) See also Ziconotide (Prialt®). Recommended after documentation of a failure of a trial of intrathecal morphine and hydromorphone. The 2007 Polyanalgesic Consensus Conference Recommendations for the Management of Pain by Intrathecal Drug Delivery concluded that ziconotide should be updated to a first-line intrathecal drug. This recommendation was published in a non peer reviewed journal and the conference was sponsored by Elan Pharmaceuticals. (Deer, 2007)

## **Intrathecal pumps**

See Implantable drug-delivery systems (IDDSs).

## **Intravenous regional sympathetic blocks (for RSD, nerve blocks) [DWC]**

Not recommended. However, if other treatments are contraindicated (e.g. when a stellate ganglion block cannot be done due to bleeding diathesis) intravenous regional blocks may be performed. IV regional blocks, also known as Bier blocks, are not commonly done for RSD. Although there is no scientific evidence to support this treatment, it is recommended as an option in certain cases when there are no other alternatives. When the procedure is performed, it must be done in conjunction with a rehabilitation program. There is no role for intravenous regional sympathetic blocks for the diagnosis of RSD.

## **Ketamine [DWC]**

Not recommended. There is insufficient evidence to support the use of ketamine for the treatment of chronic pain.

## **Ketoprofen**

See NSAIDs (non-steroidal anti-inflammatory drugs)

## **Lamotrigine (Lamictal®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Lamotrigine listing.

## **Levetiracetam (Keppra®)**

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See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Levetiracetam Listing listing.

## **Lidocaine (anesthetic)**

See CRPS, medications; CRPS, sympathetic and epidural blocks; Topical analgesics.

## **Low-Level Laser Therapy (LLLT)**

Not recommended. There has been interest in using low-level lasers as a conservative alternative to treat pain. Low-level lasers, also known as "cold lasers" and non-thermal lasers, refer to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and wattage from 5-500 milliwatts. (In contrast, lasers used in surgery typically use 300 Watts.) When applied to the skin, these lasers produce no sensation and do not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. One low-level laser device, the MicroLight 830 Laser, has received clearance for marketing from the U.S. Food and Drug Administration (FDA) specifically for the treatment of carpal tunnel syndrome. Other protocols have used low-level laser energy applied to acupuncture points on the fingers and hand. This technique may be referred to as "laser acupuncture." Given the equivocal or negative outcomes from a significant number of randomized clinical trials, it must be concluded that the body of evidence does not allow conclusions other than that the treatment of most pain syndromes with low level laser therapy provides at best the equivalent of a placebo effect. (Naeser, 2002) (Gur, 2002) (Basford, 1999) (Conti, 1997) (de Bie, 1998) (BlueCross BlueShield, 2005) Low Level Laser Therapy (LLLT) was introduced as an alternative non-invasive treatment for Osteoarthritis (OA) about 20 years ago, but its effectiveness is still controversial. For OA, the results are conflicting in different studies and may depend on the method of application and other features of the LLLT application. Despite some positive findings, data is lacking on how LLLT effectiveness is affected by four important factors: wavelength, treatment duration of LLLT, dosage and site of application over nerves instead of joints. There is clearly a need to investigate the effects of these factors on LLLT effectiveness for OA in randomized controlled clinical trials. (Brosseau-Cochrane, 2004) This meta-analysis concluded that there are insufficient data to draw firm conclusions about the effects of LLLT for low-back pain compared to other treatments, different lengths of treatment, different wavelengths and different dosages. (Yousefi-Nooraie-Cochrane, 2007)

## **Lumbar sympathetic block**

Recommended as indicated below. Useful for diagnosis and treatment of pain of the pelvis and lower extremity secondary to CRPS-I and II. This block is commonly used for differential diagnosis and is the preferred treatment of sympathetic pain involving the lower extremity. For diagnostic testing, use three blocks over a 3-14 day period. For a positive response, pain relief should be 50% or greater for the duration of the local anesthetic and pain relief should be associated with functional improvement. Should be followed by intensive physical therapy. (Colorado, 2002)

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## Magnet Therapy

Not recommended. Biomagnetic therapy is considered investigational. The data from randomized, placebo-controlled clinical trials fails to demonstrate that biomagnetic therapy results in improved health outcomes for any type of pain. Biomagnetic therapy has been proposed for the relief of chronic painful conditions; it is proposed that magnets, worn close to the skin, create an electromagnetic field within the body that suppresses pain. The theory is that the magnetic field causes potassium channels to be stimulated, producing repolarization or hyperpolarization. Biomagnetic therapy has been investigated for various types of pain, including peripheral neuropathy, chronic low back pain, carpal tunnel syndrome, plantar heel pain and hip and knee pain due to osteoarthritis. (BlueCross BlueShield, 2005)

## Manual therapy & manipulation

Recommended for chronic pain if caused by musculoskeletal conditions and manipulation is specifically recommended as an option for acute conditions. Manual Therapy is widely used in the treatment of musculoskeletal pain. The intended goal or effect of Manual Medicine is the achievement of positive symptomatic or objective measurable gains in function that facilitate progression in the patient's therapeutic exercise program and return to productive activities. Manipulation is manual therapy that moves a joint beyond the physiologic range-of-motion but not beyond the anatomic range-of-motion.

### Treatment Parameters from state guidelines

- a. Time to produce objective functional gains: 3-5 treatments
- b. Frequency: 1-5 supervised treatments per week the first 2 weeks, decreasing to 1-3 times per week for the next 6 weeks, then 1-2 times per week for the next 4 weeks, if necessary.
- c. Optimum duration: Treatment beyond 3-6 visits should be documented with objective improvement in function. Palliative care should be reevaluated and documented at each treatment session. (Colorado, 2003)

## Marijuana

See Cannabinoids

## Medications for acute pain (analgesics)

Recommended as indicated below. Pharmacologic agents are the main treatment of acute pain. Acetaminophen is the initial choice for treatment of acute pain in a dose of 1,000 mg. A recent study found that in a single dose, aspirin was similar to acetaminophen (mg to mg comparison) for treatment of acute pain, although aspirin is more likely to produce GI side effects. (Edwards, 2006) (Sachs, 2005) The maximum daily dose of acetaminophen is 4,000 mg. There should be caution about daily doses of acetaminophen and liver disease if over 4,000 mg per day or in combination with other NSAIDs. (Watkins, 2006)

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NSAIDs are superior to acetaminophen for some types of pain, and can provide analgesia similar to opioids in some settings, including post-operatively. (Mason, 2006) They suffer from a ceiling effect above which no additional analgesic effect can be obtained. They also suffer from side effects such as GI disturbance, renal dysfunction, increased edema, and increased blood pressure. NSAIDs, and the Cox-2 NSAIDs in particular, also are associated with thrombotic cardiovascular events.

Opioids are appropriate analgesics for somatic, neuropathic and visceral pain. Hydrocodone is considered the most potent oral opioid that does not require special documentation for prescribing in some states (not including California). (Quigley, 2006) Side effects include sedation, nausea, vomiting and constipation. There is no evidence that supports the addition of pentazocine (Talwin) or butorphanol (Stadol) to decrease side effects. (Sachs, 2005) This study found a negative association between receipt of early opioids for acute LBP and outcomes (disability duration, medical costs, subsequent surgery), but severity was also a strong predictor (confounding variable) of all the outcomes and may explain the early opioid use. (Webster, 2007) Tramadol is not recommended as a first-line oral analgesic because of its inferior efficacy to a combination of Hydrocodone/ acetaminophen. There is also no evidence that it has a safer adverse event profile. (Turturro, 1998)

### Medications for subacute & chronic pain

There are few studies of the use of medications in the subacute period (7 to 12 weeks) or chronic period of pain treatment. Relief of pain with the use of medications is generally temporary, and measures of the lasting benefit from this modality should include evaluating the effect of pain relief in relationship to improvements in function and increased activity. Before prescribing any medication for pain the following should occur: (1) determine the aim of use of the medication; (2) determine the potential benefits and adverse effects; (3) determine the patient's preference. Only one medication should be given at a time, and interventions that are active and passive should remain unchanged at the time of the medication change. A trial should be given for each individual medication. Analgesic medications should show effects within 1 to 3 days, and the analgesic effect of antidepressants should occur within 1 week. A record of pain and function with the medication should be recorded. (Mens, 2005) The recent AHRQ review of comparative effectiveness and safety of analgesics for osteoarthritis concluded that each of the analgesics was associated with a unique set of benefits and risks, and no currently available analgesic was identified as offering a clear overall advantage compared with the others. (Chou, 2006) There are multiple medication choices in the Procedure Summary. See Anticonvulsants for chronic pain; Antidepressants for chronic pain; Antidepressants for neuropathic pain; Antidepressants for non-neuropathic pain; Anti-Inflammatories; Benzodiazepines; Boswellia Serrata Resin (Frankincense); Cannabinoids; Capsaicin; Cod liver oil; Curcumin (Turmeric); Cyclobenzaprine (Flexeril®); Duloxetine (Cymbalta®); Gabapentin (Neurontin®); Glucosamine (and Chondroitin Sulfate); Green tea; Herbal medicines; Implantable drug-delivery systems (IDDSs); Injection with anaesthetics and/or steroids; Intrathecal drug delivery systems, medications; Intravenous regional sympathetic blocks (for RSD, nerve blocks); Ketamine; Methadone; Milnacipran (Ixel®); Muscle relaxants; Nonprescription medications; NSAIDs (non-steroidal anti-inflammatory drugs); NSAIDs, GI symptoms & cardiovascular risk; Opioids (with links to multiple topics on opioids); Pycnogenol (maritime pine bark); Salicylate topicals;

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Topical analgesics; Uncaria Tomentosa (Cat's Claw); Venlafaxine (Effexor®); White willow bark; & Ziconotide (Prialt®).

## Metaxalone (Skelaxin®)

See Muscle Relaxants

## Methadone

Recommended for moderate to severe pain. The FDA reports that they have received reports of severe morbidity and mortality with this medication. This appears, in part, secondary to the long half-life of the drug (8-59 hours). Pain relief on the other hand only lasts from 4-8 hours. Vigilance is suggested in treatment initiation, conversion from another opioid to methadone, and when titrating the methadone dose. One severe side effect is respiratory depression (which persists longer than the analgesic effect). Methadone should be given with caution to patients with decreased respiratory reserve (asthma, COPD, sleep apnea, severe obesity). QT prolongation with resultant serious arrhythmia has also been noted. Use methadone carefully in patients with cardiac hypertrophy and in patients at risk for hypokalemia (including those patients on diuretics). Methadone does have the potential for abuse.

Steps for prescribing methadone:

### (1) Basic rules

- Weigh the risks and benefits before prescribing methadone.
- Avoid prescribing 40 mg Methadone tablets for chronic non-malignant pain. This product is only FDA-approved for detoxification and maintenance of narcotic addiction.
- Closely monitor patients who receive methadone, especially during treatment initiation and dose adjustments.
- 

### (2) Know the information that is vital to give the patient:

- Don't be tempted to take more methadone than prescribed if you are not getting pain relief. This can lead to a dangerous build-up that can cause death.
- All changes in methadone dose should be made by your treating practitioner.
- Methadone can make your breath slow down, or actually stop.
- Methadone can slow down your heartbeat and you might not be able to detect this.
- If you feel like you are having an irregular heartbeat, dizziness, light-headedness or fainting, call your doctor or clinic immediately. (FDA, 2006)

### (3) Be familiar with the current SAMHSA health advisory on methadone:

- The medication has become more accessible to unauthorized users.
- It can accumulate in potentially harmful doses (especially during the first few days of treatment).
- There has been a rise in Methadone-associated mortality. (SAMHSA, 2004)

### (4) Be familiar with the FDA final policy statement on Methadone that explicitly discusses the topic, "Can Methadone be used for pain control?"

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No separate registration is required to prescribe methadone for treatment of pain. (DEA, 2006)

(5) Read the new prescribing information for Methadone and the new patient information section. (Roxane, 2006)

## **Microcurrent electrical stimulation (MENS devices) [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **Milnacipran (Ixel®) [DWC]**

Not Recommended. It is not FDA approved and not available in the US.

## **Morphine pumps**

See Implantable pumps for narcotics.

## **Multidisciplinary pain programs**

See Chronic pain programs.

## **Muscle relaxants**

Recommend non-sedating muscle relaxants with caution as a second-line option for acute LBP and for short-term pain relief in patients with chronic LBP, but benzodiazepines are not recommended. (Mens, 2005) (Van Tulder, 1998) (van Tulder, 2006) (Schnitzer, 2004) Muscle relaxants are a broad range of medications that are generally divided into antispasmodic and antispasticity drugs. (van Tulder, 2006) Antispasmodics are used to decrease muscle spasm in conditions such as LBP. These can be benzodiazepines (See Benzodiazepines) and non-benzodiazepines. Antispasticity drugs are used to decrease spasticity in conditions such as cerebral palsy, MS, and spinal cord injuries. These latter drugs block the sarcoplasmic reticulum calcium channel. Muscle relaxants may be effective in reducing pain and muscle tension, and increasing mobility. However, in most LBP cases, they show no benefit beyond NSAIDs in pain and overall improvement. Also there is no additional benefit shown in combination with NSAIDs. Efficacy appears to diminish over time, and prolonged use of some medications in this class may lead to dependence. (Homik, 2004) Sedation is the most commonly reported adverse effect of muscle relaxant medications. These drugs should be used with caution in patients driving motor vehicles or operating heavy machinery. Metaxalone (Skelaxin®) is reported to be a relatively non-sedating muscle relaxant. Carisoprodol (Soma®) is metabolized to meprobamate, an anxiolytic. There is a school of thought that its main effect is due to generalized sedation. Withdrawal symptoms may occur with abrupt discontinuation. (Reeves, 2003) See Weaning of medications. Soma has been noted to be a street drug of abuse and is often combined with acetaminophen and codeine, a combination labeled as “Soma-Coma”. (Schears, 2004) Cyclobenzaprine (Flexeril®) has similar effects to tricyclic antidepressants. It has a central mechanism of action, but it is not effective in treating spasticity from cerebral palsy

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or spinal cord disease. See Cyclobenzaprine. Muscle relaxants are effective in acute LBP. Cyclobenzaprine is associated with a number needed to treat of 3 at 2 weeks for symptom improvement and is associated with drowsiness and dizziness. Carisoprodol is also effective but has abuse and dependency potential. Metaxalone and low-dose cyclobenzaprine have fewer adverse effects. (Kinkade, 2007)\

## **Naproxen**

See Anti-inflammatory medications

## **Narcotics**

See Opioids

## **Norepinephrine serotonin reuptake inhibitors (NSRIs)**

See Duloxetine (Cymbalta®); & Milnacipran (Ixel®)

## **Neuromodulation devices**

See Spinal cord stimulators

## **Neuromuscular electrical stimulation (NMES devices) [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **Neurontin®**

See Gabapentin

## **Nonprescription medications**

Recommended. Acetaminophen (safest); NSAIDs (aspirin, ibuprofen). (Bigos, 1999) There should be caution about daily doses of acetaminophen and liver disease if over 4 g/day or in combination with other NSAIDs. (Watkins, 2006) See also NSAIDs (non-steroidal anti-inflammatory drugs).

## **NSAIDs (non-steroidal anti-inflammatory drugs)**

Recommended for acute pain, acute LBP, short-term pain relief in chronic LBP, and short-term improvement of function in chronic LBP. There is no evidence of long-term effectiveness for pain or function. There is conflicting evidence that NSAIDs are more effective than acetaminophen for acute LBP. (van Tulder, 2006) There is inconsistent evidence for the use of these medications to treat long-term neuropathic pain, but they may be useful to treat breakthrough pain in this condition. (Namaka, 2004) See NSAIDs, GI symptoms & cardiovascular risk. See also Anti-inflammatory medications and Medications for acute pain (analgesics).

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Besides the above well-documented side effects of NSAIDs, there are other less well-known effects of NSAIDs, and the use of NSAIDs has been shown to possibly delay and hamper healing in all the soft tissues, including muscles, ligaments, tendons, and cartilage. (Maroon, 2006)

### **NSAIDs, GI symptoms & cardiovascular risk**

Recommend with precautions as indicated below.

Clinicians should weight the indications for NSAIDs against both GI and cardiovascular risk factors.

Determine if the patient is at risk for gastrointestinal events: (1) age > 65 years; (2) history of peptic ulcer, GI bleeding or perforation; (3) concurrent use of ASA, corticosteroids, and/or an anticoagulant; or (4) high dose/multiple NSAID (e.g., NSAID + low-dose ASA). Recent studies tend to show that H. Pylori does not act synergistically with NSAIDS to develop gastroduodenal lesions.

Patients with no risk factor and no cardiovascular disease: Non-selective NSAIDs OK (e.g, ibuprofen, naproxen, etc.)

Patients at intermediate risk for gastrointestinal events and no cardiovascular disease: (1) A non-selective NSAID with either a PPI (Proton Pump Inhibitor, for example, 20 mg omeprazole daily) or misoprostol (200 µg four times daily) or (2) a Cox-2 selective agent. Long-term PPI use (> 1 year) has been shown to increase the risk of hip fracture (adjusted odds ratio 1.44).

Patients at high risk for gastrointestinal events with no cardiovascular disease: A Cox-2 selective agent plus a PPI if absolutely necessary. (Laine, 2006) (Scholmerich, 2006) (Nielsen, 2006) (Chan, 2004) (Gold, 2007)

Cardiovascular disease: A non-pharmacological choice should be the first option in patients with cardiac risk factors. It is then suggested that acetaminophen or aspirin be used for short-term needs. An opioid also remains a short-term alternative for analgesia. If long-term or high-dose therapy is required, naproxen appears to be the preferred choice of NSAID. Progressive medications include introducing an NSAID with Cox-2 activity. Cardiovascular risk does appear to extend to all non-aspirin NSAIDs, with the highest risk found for the Cox-2 agents. (Johnsen, 2005) (Lanas, 2006) (Antman, 2007)

Use with Aspirin for cardioprotective effect: The GI protective effect of Cox-2 agents is diminished in patients taking low-dose aspirin. (Laine, 2007) Ibuprofen appears to attenuate the antiplatelet effect of enteric-coated aspirin and should be taken 30 minutes after ASA or 8 hours before. (Antman, 2007)

Use of NSAIDs and SSRIs: The concurrent use of SSRIs and NSAIDs is associated with moderate excess relative risk of serious upper GI events when compared to NSAIDs alone. This risk was higher for non-selective NSAIDs when compared to Cox-2 selective agents (adjusted odds ratio of 1.77 and 1.33, respectively). (Helin-Salmivaara, 2007)

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## **Nucleoplasty**

Not recommended. Given the extremely low level of evidence available for Nucleoplasty (Coblation Nucleoplasty), and the lack of clinical trials, it is recommended that this procedure be regarded as experimental at this time. (Manchikanti, 2003) (Boswell, 2007) (ArthroCare Corp, Sunnyvale, CA, introduced the Micro DisCoblator in 2003 to enable minimally invasive disc decompression. Total 2003 Revenue \$119 million. Company literature: “The Nucleoplasty procedure uses a minimally-invasive catheter to create a pathway into the disc. Radio wave signals are sent through the transmitter into the nucleus of the herniated disc. The radio waves produce a low-temperature ionized gas that breaks up molecular bonds in the spongy nucleus, removing tissue volume. The Nucleoplasty procedure uses an FDA-cleared device, and is a clinically proven treatment with over 20,000 patients treated.”)

Number needed to treat (NNT) Recommended as a measure of absolute risk in evaluating drug therapies. This is the average number of patients that need to be treated in order to have improvement in one patient. As an example, for every 4 patients treated with neuropathic pain, pain relief described as good is found in 1 patient. The NNT is a useful and relatively simple tool for practicing evidence-based medicine. This calculation can be applied to intervention studies and reflects the number of additional patients who need to receive an intervention to prevent 1 additional outcome. In this recent study, using NNT was superior to achieve participant consent versus other explanations. (Halvorsen, 2007)

## **Occupational therapy (OT) [DWC]**

See Physical Medicine [ODG].

## **Omega-3 EFAs**

See Cod liver oil

## **Oral morphine**

Not recommended as a primary treatment. The use of opioid analgesics for chronic non-cancer pain is controversial. One randomized controlled trial found that oral morphine may confer analgesic benefit with a low risk of addiction but is unlikely to yield psychological or functional improvement. (Moulin, 1996) See also Opioids.

## **Opioids**

This topic is covered under multiple headings. See more specific entries, as follows: Opioids, criteria for use; Opioids for chronic pain; Opioids for neuropathic pain; Opioids for osteoarthritis; Opioids, cancer pain vs. nonmalignant pain; Opioids, dealing with misuse & addiction; Opioids, differentiation: dependence & addiction; Opioids, indicators for addiction; Opioids, long-term assessment; Opioids, pain treatment agreement; Opioids, psychological intervention; Opioids, screening for risk of addiction (tests); Opioids, state medical boards

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guidelines; Opioids, steps to avoid misuse/addiction; Detoxification; Substance abuse (tolerance, dependence, addiction); Weaning of medications; Implantable drug-delivery systems (IDDSs); Methadone; Rapid detox; Testosterone replacement for hypogonadism (related to opioids); & Opioid hyperalgesia.

## **Opioids, California Controlled Substance Utilization Review and Evaluation System (CURES) [DWC]**

For patients with risk factors for drug abuse, a treating physician may consider utilizing the Controlled Substance Utilization Review and Evaluation System (CURES, <http://ag.ca.gov/bne/trips.htm>). CURES was established to automate the collection and analysis of all Schedule II controlled substance prescriptions issued in California. A physician may request a search for a Schedule II prescription history for a specific patient.

### **Opioids, criteria for use**

#### Therapeutic Trial of Opioids

1) Establish a Treatment Plan. The use of opioids should be part of a treatment plan that is tailored to the patient. Questions to ask prior to starting therapy:

(a) Are there reasonable alternatives to treatment, and have these been tried?

(b) Is the patient likely to improve? Examples: Was there improvement on opioid treatment in the acute and subacute phases? Were there trials of other treatment, including non-opioid medications?

(c) Is there likelihood of abuse or an adverse outcome? See Substance abuse (tolerance, dependence, addiction).

(d) Ask about Red Flags indicating that opioids may not be helpful in the chronic phase: (1) Little or no relief with opioid therapy in the acute and subacute phases. (2) The patient has had a psychological evaluation and has been given a diagnosis of somatoform disorder. (3) The patient has been given a diagnosis in one of the particular diagnostic categories that have not been shown to have good success with opioid therapy: conversion disorder; somatization disorder; pain disorder associated with psychological factors (such as anxiety or depression).

(e) When the patient is requesting opioid medications for their pain and inconsistencies are identified in the history, presentation, behaviors or physical findings, physicians and surgeons who make a clinical decision to withhold opioid medications should document the basis for their decision.

2) Steps to Take Before a Therapeutic Trial of Opioids:

(a) Attempt to determine if the pain is nociceptive or neuropathic. Also attempt to determine if there are underlying contributing psychological issues. Neuropathic pain may require higher

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doses of opioids, and opioids are not generally recommended as a first-line therapy for some neuropathic pain.

(b) A therapeutic trial of opioids should not be employed until the patient has failed a trial of non-opioid analgesics.

(c) Before initiating therapy, the patient should set goals, and the continued use of opioids should be contingent on meeting these goals.

(d) Baseline pain and functional assessments should be made. Function should include social, physical, psychological, daily and work activities, and should be performed using a validated instrument or numerical rating scale. See Function Measures.

(e) Pain related assessment should include history of pain treatment and effect of pain and function.

(f) Assess the likelihood that the patient could be weaned from opioids if there is no improvement in pain and function.

(g) The patient should have at least one physical and psychosocial assessment by the treating doctor (and a possible second opinion by a specialist) to assess whether a trial of opioids should occur. When subjective complaints do not correlate with imaging studies and/or physical findings and/or when psychosocial issue concerns exist, a second opinion with a pain specialist and a psychological assessment should be obtained.

(h) The physician and surgeon should discuss the risks and benefits of the use of controlled substances and other treatment modalities with the patient, caregiver or guardian.

(i) A written consent or pain agreement for chronic use is not required but may make it easier for the physician and surgeon to document patient education, the treatment plan, and the informed consent. Patient, guardian, and caregiver attitudes about medicines may influence the patient's use of medications for relief from pain. See Guidelines for Pain Treatment Agreement. This should include the consequences of non-adherence.

(j) Consider the use of a urine drug screen to assess for the use or the presence of illegal drugs.

### 3) Initiating Therapy

(a) Intermittent pain: Start with a short-acting opioid trying one medication at a time.

(b) Continuous pain: extended-release opioids are recommended. Patients on this modality may require a dose of “rescue” opioids. The need for extra opioid can be a guide to determine the sustained release dose required.

(c) Only change 1 drug at a time.

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(d) Prophylactic treatment of constipation should be initiated.

(e) If partial analgesia is not obtained, opioids should be discontinued.

### 4) On-Going Management. Actions Should Include:

(a) Prescriptions from a single practitioner taken as directed, and all prescriptions from a single pharmacy.

(b) The lowest possible dose should be prescribed to improve pain and function.

(c) Office: Ongoing review and documentation of pain relief, functional status, appropriate medication use, and side effects. Pain assessment should include: current pain; the least reported pain over the period since last assessment; average pain; intensity of pain after taking the opioid; how long it takes for pain relief; and how long pain relief lasts. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function, or improved quality of life. Information from family members or other caregivers should be considered in determining the patient's response to treatment. The 4 A's for Ongoing Monitoring: Four domains have been proposed as most relevant for ongoing monitoring of chronic pain patients on opioids: pain relief, side effects, physical and psychosocial functioning, and the occurrence of any potentially aberrant (or nonadherent) drug-related behaviors. These domains have been summarized as the "4 A's" (analgesia, activities of daily living, adverse side effects, and aberrant drug-taking behaviors). The monitoring of these outcomes over time should affect therapeutic decisions and provide a framework for documentation of the clinical use of these controlled drugs. (Passik, 2000)

(d) Home: To aid in pain and functioning assessment, the patient should be requested to keep a pain diary that includes entries such as pain triggers, and incidence of end-of-dose pain. It should be emphasized that using this diary will help in tailoring the opioid dose. This should not be a requirement for pain management.

(e) Use of drug screening or inpatient treatment with issues of abuse, addiction, or poor pain control.

(f) Documentation of misuse of medications (doctor-shopping, uncontrolled drug escalation, drug diversion).

(g) Continuing review of overall situation with regard to nonopioid means of pain control.

(h) Consideration of a consultation with a multidisciplinary pain clinic if doses of opioids are required beyond what is usually required for the condition or pain does not improve on opioids in 3 months. Consider a psych consult if there is evidence of depression, anxiety or irritability. Consider an addiction medicine consult if there is evidence of substance misuse.

### 5) Recommended Frequency of Visits While in the Trial Phase (first 6 months):

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(a) Every 2 weeks for the first 2 to 4 months

(b) Then at approximate 1 ½ to 2-month intervals

Note: According to the California Medical Board Guidelines for Prescribing Controlled Substances for Pain, patients with pain who are managed with controlled substances should be seen monthly, quarterly, or semiannually as required by the standard of care. (California, 1994)

6) When to Discontinue Opioids: See Opioid hyperalgesia. Also see Weaning of Medications. Prior to discontinuing, it should be determined that the patient has not had treatment failure due to causes that can be corrected such as under-dosing or inappropriate dosing schedule. Weaning should occur under direct ongoing medical supervision as a slow taper except for the below mentioned possible indications for immediate discontinuation. The patient should not be abandoned.

(a) If there is no overall improvement in function, unless there are extenuating circumstances

(b) Continuing pain with the evidence of intolerable adverse effects

(c) Decrease in functioning

(d) Resolution of pain

(e) If serious non-adherence is occurring

(f) The patient requests discontinuing

(g) Immediate discontinuation has been suggested for: evidence of illegal activity including diversion, prescription forgery, or stealing; the patient is involved in a motor vehicle accident and/or arrest related to opioids, illicit drugs and/or alcohol; intentional suicide attempt; aggressive or threatening behavior in the clinic. It is suggested that a patient be given a 30-day supply of medications (to facilitate finding other treatment) or be started on a slow weaning schedule if a decision is made by the physician to terminate prescribing of opioids/controlled substances.

(h) Many physicians will allow one “slip” from a medication contract without immediate termination of opioids/controlled substances, with the consequences being a re-discussion of the clinic policy on controlled substances, including the consequences of repeat violations.

(i) If there are repeated violations from the medication contract or any other evidence of abuse, addiction, or possible diversion it has been suggested that a patient show evidence of a consult with a physician that is trained in addiction to assess the ongoing situation and recommend possible detoxification. (Weaver, 2002)

(j) When the patient is requesting opioid medications for their pain and inconsistencies are identified in the history, presentation, behaviors or physical findings, physicians and surgeons

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who make a clinical decision to withhold opioid medications should document the basis for their decision.

### 7) When to Continue Opioids

(a) If the patient has returned to work

(b) If the patient has improved functioning and pain

(Washington, 2002) (Colorado, 2002) (Ontario, 2000) (VA/DoD, 2003) (Maddox-AAPM/APS, 1997) (Wisconsin, 2004) (Warfield, 2004)

### Opioids for chronic pain

Neuropathic pain: See Opioids for neuropathic pain.

Nociceptive pain: Recommended as the standard of care for treatment of moderate or severe nociceptive pain (defined as pain that is presumed to be maintained by continual injury with the most common example being pain secondary to cancer).

Chronic pain can have a mixed physiologic etiology of both neuropathic and nociceptive components. In most cases, analgesic treatment should begin with acetaminophen, aspirin, and NSAIDs (as suggested by the WHO step-wise algorithm). When these drugs do not satisfactorily reduce pain, opioids for moderate to moderately severe pain may be added to (not substituted for) the less efficacious drugs. A major concern about the use of opioids for chronic pain is that most randomized controlled trials have been limited to a short-term period ( $\leq 70$  days). This leads to a concern about confounding issues such as tolerance, opioid-induced hyperalgesia, long-range adverse effects such as hypogonadism and/or opioid abuse, and the influence of placebo as a variable for treatment effect. (Ballantyne, 2006) (Furlan, 2006) Long-term, observational studies have found that treatment with opioids tends to provide improvement in function and minimal risk of addiction, but many of these studies include a high dropout rate (56% in a 2004 meta-analysis). (Kalso, 2004) There is also no evidence that opioids showed long-term benefit or improvement in function when used as treatment for chronic back pain. (Martell-Annals, 2007) Current studies suggest that the “upper limit of normal” for opioids prior to evaluation with a pain specialist for the need for possible continuation of treatment, escalation of dose, or possible weaning, is in a range from 120-180 mg morphine equivalents a day. (Ballantyne, 2006) (AMDG, 2007)

There are several proposed guidelines for the use of opioids for chronic non-malignant pain, but these have not been evaluated in clinical practice, and selection of the patient that will best respond to this treatment modality remains difficult. (Nicholas, 2006) (Stein, 2000) One of the most recent of these guidelines is the Agency Medical Director’s Group (AMDG) Guidelines from Washington State. This guideline includes an opioid dosing calculator. (AMDG, 2007)

Outcomes measures: It is now suggested that rather than simply focus on pain severity, improvements in a wide range of outcomes should be evaluated, including measures of functioning, appropriate medication use, and side effects. Measures of pain assessment that allow

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for evaluation of the efficacy of opioids and whether their use should be maintained include the following: current pain; the least reported pain over the period since last assessment; average pain; intensity of pain after taking the opioid; how long it takes for pain relief; and how long pain relief lasts. (Nicholas, 2006) (Ballantyne, 2006) A recent epidemiologic study found that opioid treatment for chronic non-malignant pain did not seem to fulfill any of key outcome goals including pain relief, improved quality of life, and/or improved functional capacity. (Eriksen, 2006)

Tolerance and addiction: Opioid tolerance develops with the repeated use of opioids and brings about the need to increase the dose and may lead to sensitization. It is now clear that analgesia may not occur with open-ended escalation of opioids. It has also become apparent that analgesia is not always sustained over time, and that pain may be improved with weaning of opioids. (Ballantyne, 2006) (Ballantyne, 2003) See Substance abuse (tolerance, dependence, addiction).

Behavior reinforcement: A major concern in the use of opioids has been that a focus on this treatment without coordination with other modalities, such as psychosocial or behavioral therapy, may simply reinforce pain-related behavior, ultimately undermining rehabilitation that has been targeted at functional restoration. (Ontario, 2000) It has been shown that pain behavior can be reinforced by the prescribing of opioids, generally on an unintentional basis by the patient. (Fordyce, 1991)

Overall treatment suggestions: Current guidelines suggest the following:

- A trial of opioids as a first step in treatment, and the steps involved are outlined in the Criteria for Use of Opioids. The trial includes an initiation phase that involves selection of the opioid and initial dose. (VA/DoD, 2003)
- There is then a titration phase that includes dose adjustment. At this phase it may be determined that opioids are not achieving the desired outcomes, and they should be discontinued.
- The final stage is the maintenance phase. If pain worsens during this phase the differential to evaluate includes disease progression, increased activity, and/or new or increased pre-existing psychosocial factors that influence pain. In addition, the patient may develop hyperalgesia, tolerance, dependence or actual addiction.

Recommendations for general conditions:

- Neuropathic pain: Opioids have been suggested for neuropathic pain that has not responded to first-line recommendations (antidepressants, anticonvulsants).
- Chronic back pain: Appear to be efficacious for short-term pain relief, but long-term efficacy is unclear (>16 weeks). In patients taking opioids for back pain, the prevalence of lifetime substance use disorders has ranged from 36% to 56% (but the author warns that these statistics are limited by poor study design and publication bias). (Martell-Annals, 2007)
- Mechanical and compressive etiologies: rarely beneficial

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- Headaches: not recommended.

- Osteoarthritis: Not recommended as a first-line therapy. Recommended on a trial basis for short-term use after there has been evidence of failure of first-line medication options such as acetaminophen or NSAIDs when there is evidence of moderate to severe pain. Also recommended for a trial if there is evidence of contraindications for use of first-line medications. Under study for long-term use a there is a lack of evidence to allow for a treatment recommendation. If used on a long-term basis, the criteria for use of opioids should be followed. See Opioids for osteoarthritis for citations.

(Washington, 2002) (Colorado, 2002) (Ontario, 2000) (VA/DoD, 2003) (Maddox-AAPM/APS, 1997) (Wisconsin, 2004) (Warfield, 2004) See Substance abuse (tolerance, dependence, addiction). See also Implantable pumps for narcotics. See also Opioids in the Low Back Chapter. See Criteria for Use of Opioids.

## **Opioids for neuropathic pain**

Not recommended as a first-line therapy. There is limited assessment of effectiveness of opioids for neuropathic pain, with short-term studies showing contradictory results and intermediate studies (8-70 days) demonstrating efficacy. (Eisenberg-Cochrane, 2006) (Eisenberg-JAMA, 2005) The results of short-term trials were mixed with respect to analgesia (less than 24 hours of treatment). Intermediate trials (average treatment duration of 28 days) showed statistical significance for reducing neuropathic pain by 20% to 30% (and 30% may be the threshold for describing a meaningful reduction of pain). Opioids may be a safer choice for patients with cardiac and renal disease than antidepressants or anticonvulsants. (Namaka, 2004) Morphine: superior to placebo in post-herpetic neuralgia, phantom limb and painful diabetic neuropathy (number needed to treat of 2.5). Oxycodone: post-herpetic neuralgia and painful diabetic neuropathy (NNT of 2.6). Tramadol: 2 trials of painful polyneuropathy on trial of post-herpetic neuropathy (overall NNT of 3.9). (Finnerup, 2005)

## **Opioids for osteoarthritis**

Not recommended as a first-line therapy. Recommended on a trial basis for short-term use after there has been evidence of failure of first-line medication options such as acetaminophen or NSAIDs when there is evidence of moderate to severe pain. Also recommended for a trial if there is evidence of contraindications for use of first-line medications. (Stitik, 2006) (Avouac, 2007) Under study for long-term use. There is a lack of evidence to allow for a treatment recommendation. If used on a long-term basis, the criteria for use of opioids should be followed. See Opioids, criteria for use.

Opioids in general: A recent meta-analysis found that opioids were more effective than placebo for reducing pain intensity. The benefit for physical function was small and was considered questionable for clinical relevance. Lack of benefit for function may be due to lack of anti-inflammatory effect for this class of medications and presence of side effects such as dizziness and drowsiness. Adverse events in general may limit the benefit of opioids as this same study found that out of every five patients that received opioids, one discontinued the medication due

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to an adverse event. These adverse events included epigastric pain, nausea, vomiting, constipation, dry mouth, dizziness, somnolence and headache. Weaker opioids were found to be less likely to produce adverse effects than stronger opioids such as oxycodone, Fentanyl or morphine. No conclusion can be made on how opioids compare to other available pharmacologic treatment due to limited studies. (Avouac, 2007)

Tramadol: A recent Cochrane review found that this drug decreased pain intensity, produced symptom relief and improved function for a time period of up to three months but the benefits were small (a 12% decrease in pain intensity from baseline). Adverse events often caused study participants to discontinue this medication, and could limit usefulness. There are no long-term studies to allow for recommendations for longer than three months. (Cepeda, 2006)

### **Opioids, cancer pain vs. nonmalignant pain**

Definition. The use of opioids is well accepted in treating cancer pain, where nociceptive mechanisms are generally present due to ongoing tissue destruction, expected survival may be short, and symptomatic relief is emphasized more than functional outcomes. In chronic non-malignant pain, by contrast, tissue destruction has generally ceased. Expected survival in chronic pain is relatively long and return to a high level of function is a major goal of treatment. Therefore, approaches to pain developed in the context of malignant pain may not be transferable to chronic non-malignant pain. See Opioids for chronic pain.

### **Opioids, dealing with misuse & addiction**

Recommend that, if there are active signs of misuse, these concerns should be addressed immediately with the patient. If there are active signs of relapse to addiction, or new-onset addiction, these patients should be referred to an addictionologist immediately. It has been suggested that most chronic pain problems will not resolve while there is active and ongoing alcohol, illicit drug, or prescription drug abuse. (Weaver, 2002) Many physicians will allow one “slip” from a medication contract without immediate termination of opioids/controlled substances, with the consequences being a re-discussion of the clinic policy on controlled substances, including the consequences of repeat violations. If there are repeated violations from the medication contract or any other evidence of abuse, addiction, or possible diversion, it has been suggested that a patient show evidence of consultation with a physician trained in addiction treatment for assessment of the situation and possible detoxification. It is also suggested that a patient be given a 30-day supply of medications (to facilitate finding other treatment) or be started on a slow weaning schedule if a decision is made by the physician to terminate prescribing of opioids/controlled substances. (Weaver, 2002) When less serious warning signs arise, the following have been recommended (after making sure that there is no change in the patient’s condition that has introduced a need for additional treatment): (a) Initiate closer monitoring with more frequent visits; (b) Consider limitations in the amount of medication prescribed at any one time; & (c) Re-review the clinic policy on controlled substance use and the medication contract. (Weaver, 2002) (Chabel, 1997) In situations where there is dual diagnosis of opioid dependence and intractable pain, both of which are being treated with controlled substances, protections apply to California physicians and surgeons who prescribe controlled substances for intractable pain provided the physician complies with the requirements of the

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general standard of care and California Business and Professions Code section 2241.5. (California, 1994)

## **Opioids, differentiation: dependence & addiction**

Recommend screening to differentiate between dependence and addiction with opioids. The screening instruments below have been developed or are in the development stages to aid in differentiation between drug dependence and addiction. See also Opioids, red flags for addiction; Opioids, screening for risk of addiction; Opioids, patients at high-risk for misuse; & Substance abuse (tolerance, dependence, addiction).

1) The Prescription Drug Use Questionnaire: (Compton, 1998) This is a tool still in development, and it has not been validated. Variables found to be positive for individuals with a substance disorder were the following: (a) Belief by the individual that he/she was addicted; (b) Drug seeking behaviors (having more than one provider, increasing analgesic dose or frequency, calling in for early refills, and obtaining analgesics from the ER); (c) Using analgesics to relieve symptoms other than pain (insomnia, anxiety, depression); (d) supplementing analgesics with alcohol or other psychoactive drugs; & (e) Having been terminated from care by a physician or dentist. The three variables that correctly classified > 90% of addicts were: (1) A tendency to consider oneself addicted; (2) A preference for the route of administration; & (3) A tendency to increase opioid dose.

2) Prescription opiate abuse in chronic pain patients (A NIH workshop summary): (Chabel, 1997) These criteria were developed to define prescription opiate abuse in patients using long-term opiates to treat chronic pain. Opiate abusers had at least three of the five of the following positive variables: (a) An overwhelming focus on opiate issues (persisting beyond the 3rd treatment session); (b) a pattern of early refills (3 or more) or escalating drug use in the absence of acute changes; (c) Multiple phone calls are made to the office for more opiates, early refills, or problems filling a previous prescription; (d) There is a pattern of prescription problems (lost medications, spilled medications, stolen medications); & (e) There is evidence of supplemental sources of opiates (multiple providers, emergency rooms, or illegal sources).

3) Chelminski multi-disciplinary pain management program criteria: (Chelminski, 2005) Criteria used to define serious substance misuse in a multi-disciplinary pain management program: (a) cocaine or amphetamines on urine toxicology screen (positive cannabinoid was not considered serious substance abuse); (b) procurement of opioids from more than one provider on a regular basis; (c) diversion of opioids; (d) urine toxicology screen negative for prescribed drugs on at least two occasions (an indicator of possible diversion); & (e) urine toxicology screen positive on at least two occasions for opioids not routinely prescribed.

4) The Pain Medication Questionnaire (PMQ): (Adams, 2004) This is a screening instrument that is in development.

5) Portenoy criteria: (Portenoy, 1997) A compiled list of “aberrant drug-related behaviors.” Those behaviors that were identified as “probably more predictive” included: (a) forging

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prescriptions; (b) Stealing or borrowing drugs from others; (c) Frequent loss of prescriptions; & (d) Revisiting change to pain treatment (especially in light of adverse side effects).

6) Michna - Predicting aberrant drug behavior based on abuse history: (Michna, 2004) Six aberrant behaviors identified: (a) multiple unsanctioned escalations in dose; (b) lost or stolen medication; (c) frequent visits to the pain center or emergency room; (d) family members expressed concern about the patient's use of opioids; & (e) excessive numbers of calls to the clinic. Other predictive variables included: (a) family history of substance abuse; (b) past problems with drugs and alcohol; (c) history of legal problems; (d) higher required dose of opioids for pain; (e) dependence on cigarettes; (f) psychiatric treatment history; (g) multiple car accidents; & (h) reporting fewer adverse symptoms from opioids.

### **Opioids, indicators for addiction**

Recommend screening for indicators below. It is estimated that the prevalence of addictive disorders and/or serious substance misuse in patients with chronic pain may be as high as 30%. (Chelminski, 2005) The prevalence of current substance abuse disorders in patients with chronic back pain ranges from 3% to 43%, with a lifetime prevalence of 54% (but the author warns that these statistics are limited by poor study design and publication bias). (Martell-Annals, 2007) In studies of patients in methadone maintenance treatment as many as 44% of patients with chronic pain felt that the use of prescription opioids led to their problems with addiction. (Jamison, 2000) One particular problem is that in patients with substance abuse disorders and chronic pain the detrimental effects of drug use on lifestyle and psychosocial function may be ascribed to chronic pain instead of drug use, making the addiction disorder difficult to diagnose and treat. In addition, intermittent substance abuse withdrawal presents as and/or may cause hyperalgesia and facilitate pain. Another problem is that physicians are not well trained in diagnosing addiction or treating this condition. (Compton, 1998). (Savage, 2002) Clinical judgment by a physician trained in recognition of addiction is needed to determine if the patient actually has an addiction disorder. A history of an addiction disorder does not preclude a patient from being treated with opioids. (Savage, 1999) (Portenoy, 1996) See also Criteria for use of opioids; Opioids, screening for risk of addiction; Opioids, screening for dependence vs. addiction; Opioids, patients at high-risk for misuse; & Substance abuse (tolerance, dependence, addiction)

Indicators and predictors of possible misuse of controlled substances and/or addiction:

1) Adverse consequences: (a) Decreased functioning, (b) Observed intoxication, (c) Negative affective state

2) Impaired control over medication use: (a) Failure to bring in unused medications, (b) Dose escalation without approval of the prescribing doctor, (c) Requests for early prescription refills, (d) Reports of lost or stolen prescriptions, (e) Unscheduled clinic appointments in "distress", (f) Frequent visits to the ED, (g) Family reports of overuse of intoxication

3) Craving and preoccupation: (a) Non-compliance with other treatment modalities, (b) Failure to keep appointments, (c) No interest in rehabilitation, only in symptom control, (d) No relief of pain or improved function with opioid therapy, (e) Overwhelming focus on opiate issues.

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4) Adverse behavior: (a) Selling prescription drugs, (b) Forging prescriptions, (c) Stealing drugs, (d) Using prescription drugs in ways other than prescribed (such as injecting oral formulations), (e) Concurrent use of alcohol or other illicit drugs (as detected on urine screens), (f) Obtaining prescription drugs from non-medical sources

(Wisconsin, 2004) (Michna, 2004) (Chabal, 1997) (Portenoy, 1997)

## Opioids, long-term assessment

### CRITERIA FOR USE OF OPIOIDS

#### Long-term Users of Opioids (6-months or more)

##### 1) Re-assess

(a) Has the diagnosis changed?

(b) What other medications is the patient taking? Are they effective, producing side effects?

(c) What treatments have been attempted since the use of opioids? Have they been effective? For how long?

(d) Document pain and functional improvement and compare to baseline. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function, or improved quality of life. Information from family members or other caregivers should be considered in determining the patient's response to treatment. Pain should be assessed at each visit, and functioning should be measured at 6-month intervals using a numerical scale or validated instrument.

(e) Document adverse effects: constipation, nausea, vomiting, headache, dyspepsia, pruritis, dizziness, fatigue, dry mouth, sweating, hyperalgesia, sexual dysfunction, and sedation.

(f) Does the patient appear to need a psychological consultation? Issues to examine would include motivation, attitude about pain/work, return-to-work, social life including interpersonal and work-related relationships.

(g) Is there indication for a screening instrument for abuse/addiction. See Substance Abuse Screening.

##### 2) Strategy for maintenance

(a) Do not attempt to lower the dose if it is working

(b) Supplemental doses of break-through medication may be required for incidental pain, end-of-dose pain, and pain that occurs with predictable situations. This can be determined by

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information that the patient provides from a pain diary or evaluation of additional need for supplemental medication.

(c) The standard increase in dose is 25 to 50% for mild pain and 50 to 100% for severe pain (Wisconsin)

## 3) Visit Frequency

(a) There is no set visit frequency. This should be adjusted to the patient's need for evaluation of adverse effects, pain status, and appropriate use of medication, with recommended duration between visits from 1 to 6 months.

(Washington, 2002) (Colorado, 2002) (Ontario, 2000) (VA/DoD, 2003) (Maddox-AAPM/APS, 1997) (Wisconsin, 2004) (Warfield, 2004)

## Opioids, pain treatment agreement

Recommended. A written consent or pain agreement for chronic use is not required but may make it easier for the physician and surgeon to document patient education, the treatment plan, and the informed consent. Patient, guardian, and caregiver attitudes about medicines may influence the patient's use of medications for relief from pain. This type of written document should be obtained prior to initiating opioid therapy. It should be discussed with the patient and family. This plan should be signed and dated and placed in the patient's chart, and include the following: (1) Goals of therapy, (2) Only one provider gives prescriptions, (3) Only one pharmacy dispenses prescriptions, (4) There will be a limit of number of medications, and dose of specific medications, (5) Medications are not to be altered without the prescribing doctor's permission, (6) Heavy machinery and automobile driving is not to occur until drug-induced sedation/drowsiness has cleared, (7) Refills are limited, and will only occur at appointments, (8) Treatment compliance must occur for all other modalities enlisted, (9) Urine drug screens may be required, (10) The patient must acknowledge that they are aware of potential adverse effects of the use of opioids including addiction, (11) Information about opioid management can be shared with family members and other providers as necessary, (12) If opioid use is not effective, the option of discontinuing this therapy may occur, (13) The consequence of non-adherence to the treatment agreement is outlined. (VA/DoD, 2003) (Heit, 2007)

## Opioids, patients at high-risk for misuse

See Opioids, steps to avoid misuse/addiction.

## Opioids, psychological intervention

Recommended as an option to improve effectiveness of opioids for chronic pain. The following steps have been suggested to improve opioid treatment: (a) Provide ongoing education on both the benefits and limitations of opioid treatment. In particular, this should be based on the patient's experience with medication treatment and behavior regarding controlled substances in general. (b) Emphasize non-opioid care including self-management techniques. These may

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include relaxation, mindfulness meditation, acceptance, and distraction. (c) Emphasize realistic goals. (d) Avoid increasing dosages of medications to “chase pain.” The result may ultimately be development of tolerance and/or hyperalgesia. (e) Encourage development of strategies for self-regulation of medication misuse. This may also include incorporation of a support group such as friends, family, an identified group (such as a 12-step group or group counseling), and/or individual counseling. (Naliboff, 2006)

### **Opioids, red flags for addiction**

See Opioids, indicators for addiction.

### **Opioids, screening for dependence vs. addiction**

See Opioids, differentiation: dependence & addiction.

### **Opioids, screening for risk of addiction (tests)**

Recommend screening for the risk of addiction prior to initiating opioid therapy. It is important to attempt to identify individuals who have the potential to develop aberrant drug use both prior to the prescribing of opioids and while actively undergoing this treatment. Most screening occurs after the claimant is already on opioids on a chronic basis, and consists of screens for aberrant behavior/misuse. Recommended screening instruments include the following:

1) The CAGE Questionnaire: (Brown, 1995) The most widely used screening tool prior to starting opioids is the CAGE questionnaire.

- a) Have you ever felt the need to cut down on your drinking or drug use?
- b) Have people annoyed you by criticizing your drinking or drug use?
- c) Have you ever felt bad or guilty about your drinking or drug use?
- d) Have you ever needed an eye opener the first thing in the morning to settle your nerves?

2) Cyr-Wartman Screen: (Cyr, 1988)

- a) Have you ever had a problem with alcohol (or drugs)?
- b) When was your last drink (or drugs)?

3) Skinner Trauma Screen (Skinner, 1984) Since your 18th birthday, have you

- a) Had any fractures or dislocations to your bones or joints?
- b) Been injured in a road traffic accident?

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- c) Injured your head?
- d) Been injured in an assault or fight (excluding injuries from sports)?
- e) Been injured after drinking?

4) The Screener and Opioid Assessment for Patients with Pain (SOAPP) (Akbik, 2006) A brief self-report measure to capture important information in order to identify which chronic pain patients may be at risk for problems with long-term opioid medications. The cutoff score has been found with a positive answer of 8 or higher. Five factors were identified on factor analysis labeled 1) history of substance abuse, 2) legal problems, 3) craving medication, 4) heavy smoking, and 5) mood swings.

It is important to note that being at risk does not necessarily indicate that a patient will develop an addiction disorder, or is addicted. A history of an addiction disorder does not preclude a patient from being treated with opioids. (Savage 1999) (Portenoy, 1996)

## **Opioids, state medical boards guidelines**

The Federation of State Medical Boards Model Guidelines for the Use of Controlled Substances for the Treatment of Pain say State medical boards recognize undertreatment of pain as a public health priority. Underprescribing pain medications is considered as much a breach of the appropriate standard of care as overprescribing. (Federation, 2004) See also individual state guidelines, for example the California Medical Board Guidelines for Prescribing Controlled Substances for Pain. (California, 1994)

## **Opioids, steps to avoid misuse/addiction**

The following are steps to avoid misuse of opioids, and in particular, for those at high risk of abuse:

- a) Opioid therapy contracts. See Guidelines for Pain Treatment Agreement.
- b) Limitation of prescribing and filling of prescriptions to one pharmacy.
- c) Frequent random urine toxicology screens.
- d) Frequent evaluation of clinical history, including questions about cravings for the former drug of abuse (a potential early sign of relapse).
- e) Frequent review of medications (including electronic medical record evaluation when available and pill counts at each visit, brought in the original bottle from the pharmacy).
- f) Communication with pharmacists.

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g) Communication with previous providers and other current providers, with evidence of obtaining medical records. (It has been recommended that opioids should not be prescribed on a first visit until this step has been undertaken.)

h) Evidence of participation in a recovery program (12-step or follow-up with a substance abuse counselor), such as speaking to his/her sponsor for the 12-step program.

i) Establishment of goals of treatment that can be realistically achieved.

j) Initiation of appropriate non-opioid adjunct medications and exercise programs.

k) Utilize careful documentation, and in particular, that which is recommended in the State in which opioids are prescribed.

l) Incorporate family and friends for support and education.

(Chabel,1997) (Michna,2004) (Weaver,2002)

### **Opioids, weaning of medications**

See Weaning of medications.

### **Opioid hyperalgesia**

Recommend screening and treatment as indicated below.

Definition: Patients who receive opiate therapy sometimes develop unexpected changes in their response to opioids. This may include the development of abnormal pain (hyperalgesia), a change in pain pattern, or persistence in pain at higher levels than expected. These types of changes occur in spite of continued incremental dose increases of medication. Opioids in this case actually increase rather than decrease sensitivity to noxious stimuli. It is important therefore to note that a decrease in opioid efficacy should not always be treated by increasing the dose, but may actually require weaning. (Chang, 2007)

Diagnosis: How to diagnose:

(1) Attempt to determine if pain has increased over that, which was pre-existing (in the absence of apparent disease progression).

(2) Attempt to determine if the patient has previously responded to opioids but now has worsening pain.

(3) Attempt to determine if the patient has never had improved pain with opioids.

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(4) If disease progression is ruled out, is there evidence of possible opioid tolerance or is this opioid hyperalgesia.

(5) Evaluate pain: In cases of opioid hyperalgesia pain may spread and become more diffuse and less well-defined in quality, beyond what would be expected from the preexisting pain state. This is generally not an acute but is an insidious process.

(6) Psychological issues such as secondary gain, exacerbation of underlying depression or anxiety, and the development of addictive disease should also be ruled out.

Treatment: Suggested treatment for patients with increasing pain (assumes that the patient has had improvement with opioids at some point):

(1) It is not unreasonable to give a trial of opioid dose escalation to see if pain and function improves. If pain improves, the diagnosis is probable tolerance. If pain does not improve or worsens, this may be evidence of opioid hyperalgesia and the opioid dose should be reduced or actually weaned.

(2) Opioid rotation is another option.

(3) Use of adjuvant pain medications is recommended when there is evidence of either tolerance or hyperalgesia.

(4) Further evaluation by a specialist with additional expertise in psychiatry, pain medicine, or addiction medicine should be considered when there is evidence of no improvement of pain with increasing doses of opioids.

## **Opioid pumps**

See Implantable drug-delivery systems (IDDSs).

## **Oxcarbazepine (Trileptal®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Oxcarbazepine listing.

## **Oxycontin® (oxycodone)**

See Opioids

## **Pain management programs**

See Chronic pain programs.

## **Percutaneous electrical nerve stimulation (PENS) [DWC]**

Not recommended.

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## **Percutaneous neuromodulation therapy (PNT)**

Not recommended. Percutaneous neuromodulation therapy (PNT) is considered investigational. Percutaneous neuromodulation therapy is a variant of PENS in which up to 10 fine filament electrodes are temporarily placed at specific anatomical landmarks in the back. Treatment regimens consist of 30-minute sessions, once or twice a week for eight to ten sessions. Percutaneous Neuromodulation Therapy™ (Vertis Neurosciences) received approval to market by the U.S. Food and Drug Administration (FDA) through the 510(k) process in 2002. The labeled indications reads as follows: "Percutaneous neuromodulation therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable pain and/or as an adjunct treatment in the management of post-surgical pain and post-trauma pain." (Condon, 2002) (BlueCross BlueShield, 2004)

## **Phentolamine infusion test**

Recommended as indicated below. An intravenous infusion of phentolamine, an alpha 2 blocker, results in generalized systemic sympatholysis. The infusion begins with intravenous saline for placebo control. For a positive response, pain relief should be 50 percent or greater and associated with functional improvement. This test aids in the diagnosis of SMP (Sympathetically maintained pain). (Colorado, 2002) See also Sympathetically maintained pain (SMP).

## **Phenytoin (Dilantin®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Phenytoin listing.

## **Phototherapy**

See Low level laser therapy (LLLT).

## **Physical Medicine [ODG]**

Recommended as indicated below. Passive therapy (those treatment modalities that do not require energy expenditure on the part of the patient) can provide short term relief during the early phases of acute pain treatment and are directed at controlling symptoms such as pain, inflammation and swelling and to improve the rate of healing soft tissue injuries. They can be used sparingly with active therapies to help control swelling, pain and inflammation during the rehabilitation process. Active therapy is based on the philosophy that therapeutic exercise and/or activity are beneficial for restoring flexibility, strength, endurance, function, range of motion, and can alleviate discomfort. Active therapy requires an internal effort by the individual to complete a specific exercise or task. This form of therapy may require supervision from a therapist or medical provider such as verbal, visual and/or tactile instruction(s). Patients are instructed and expected to continue active therapies at home as an extension of the treatment process in order to maintain improvement levels. Home exercise can include exercise with or without mechanical assistance or resistance and functional activities with assistive devices.

# CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

(Airaksinen, 2006) Patient-specific hand therapy is very important in reducing swelling, decreasing pain, and improving range of motion in CRPS. (Li, 2005)

Physical Medicine Guidelines –

- Allow for fading of treatment frequency (from up to 3 visits per week to 1 or less), plus active self-directed home Physical Medicine.
- Myalgia (muscle pain) or myositis (inflammation): 9-10 visits over 8 weeks
- Reflex sympathetic dystrophy (CRPS-I): 26 visits over 16 weeks

## Physical Therapy (PT) [DWC]

See Physical Medicine [ODG]

## Power mobility devices (PMDs)

Not recommended if the functional mobility deficit can be sufficiently resolved by the prescription of a cane or walker, or the patient has sufficient upper extremity function to propel a manual wheelchair, or there is a caregiver who is available, willing, and able to provide assistance with a manual wheelchair. Early exercise, mobilization and independence should be encouraged at all steps of the injury recovery process, and if there is any mobility with canes or other assistive devices, a motorized scooter is not essential to care.

## Pregabalin (Lyrica®)

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Pregabalin listing.

## Prialt®

See Ziconotide (Prialt®).

## Prolotherapy

Not recommended. Prolotherapy describes a procedure for strengthening lax ligaments by injecting proliferating agents/sclerosing solutions directly into torn or stretched ligaments or tendons or into a joint or adjacent structures to create scar tissue in an effort to stabilize a joint. Agents used with prolotherapy have included zinc sulfate, psyllium seed oil, combinations of dextrose, glycerine and phenol, or dextrose alone. "Proliferatives" act to promote tissue repair or growth by prompting release of growth factors, such as cytokines, or increasing the effectiveness of existing circulating growth factors. Prolotherapy has been investigated as a treatment of various etiologies of pain, including arthritis, degenerative disc disease, fibromyalgia, tendinitis, and plantar fasciitis. In all studies the effects of prolotherapy did not significantly exceed placebo effects. (BlueCross BlueShield, 2006)

## Psychological evaluations

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Recommended. Psychological evaluations are generally accepted, well-established diagnostic procedures not only with selected use in pain problems, but also with more widespread use in subacute and chronic pain populations. Diagnostic evaluations should distinguish between conditions that are preexisting, aggravated by the current injury or work related. Psychosocial evaluations should determine if further psychosocial interventions are indicated. The interpretations of the evaluation should provide clinicians with a better understanding of the patient in their social environment, thus allowing for more effective rehabilitation. (Main-BMJ, 2002) (Colorado, 2002) (Gatchel, 1995) (Gatchel, 1999) (Gatchel, 2004) (Gatchel, 2005) For the evaluation and prediction of patients who have a high likelihood of developing chronic pain, a study of patients who were administered a standard battery psychological assessment test found that there is a psychosocial disability variable that is associated with those injured workers who are likely to develop chronic disability problems. (Gatchel, 1999) Childhood abuse and other past traumatic events were also found to be predictors of chronic pain patients. (Goldberg, 1999) Another trial found that it appears to be feasible to identify patients with high levels of risk of chronic pain and to subsequently lower the risk for work disability by administering a cognitive-behavioral intervention focusing on psychological aspects of the pain problem. (Linton, 2002) Other studies and reviews support these theories. (Perez, 2001) (Pulliam, 2001) (Severeijns, 2001) (Sommer, 1998) In a large RCT the benefits of improved depression care (antidepressant medications and/or psychotherapy) extended beyond reduced depressive symptoms and included decreased pain as well as improved functional status. (Lin-JAMA, 2003) See "Psychological Tests Commonly Used in the Assessment of Chronic Pain Patients" from the Colorado Division of Workers' Compensation, which describes and evaluates the following 26 tests: (1) BHI - Battery for Health Improvement, (2) MBHI - Millon Behavioral Health Inventory, (3) MBMD - Millon Behavioral Medical Diagnostic, (4) PAB - Pain Assessment Battery, (5) MCMI-111 - Millon Clinical Multiaxial Inventory, (6) MMPI-2 - Minnesota Inventory, (7) PAI - Personality Assessment Inventory, (8) BBHI 2 - Brief Battery for Health Improvement, (9) MPI - Multidimensional Pain Inventory, (10) P-3 - Pain Patient Profile, (11) Pain Presentation Inventory, (12) PRIME-MD - Primary Care Evaluation for Mental Disorders, (13) PHQ - Patient Health Questionnaire, (14) SF 36, (15) SIP - Sickness Impact Profile, (16) BSI - Brief Symptom Inventory, (17) BSI 18 - Brief Symptom Inventory, (18) SCL-90 - Symptom Checklist, (19) BDI-II - Beck Depression Inventory, (20) CES-D - Center for Epidemiological Studies Depression Scale, (21) PDS - Post Traumatic Stress Diagnostic Scale, (22) Zung Depression Inventory, (23) MPQ - McGill Pain Questionnaire, (24) MPQ-SF - McGill Pain Questionnaire Short Form, (25) Oswestry Disability Questionnaire, (26) Visual Analogue Pain Scale - VAS. (Bruns, 2001) See also Comorbid psychiatric disorders.

### **Psychological evaluations, IDDS & SCS (intrathecal drug delivery systems & spinal cord stimulators)**

Recommended pre-intrathecal drug delivery systems (IDDS) and spinal cord stimulator (SCS) trial.

### **Psychological treatment**

Recommended for appropriately identified patients during treatment for chronic pain. Psychological intervention for chronic pain includes setting goals, determining appropriateness

# CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

of treatment, conceptualizing a patient's pain beliefs and coping styles, assessing psychological and cognitive function, and addressing co-morbid mood disorders (such as depression, anxiety, panic disorder, and posttraumatic stress disorder). Cognitive behavioral therapy and self-regulatory treatments have been found to be particularly effective. Psychological treatment incorporated into pain treatment has been found to have a positive short-term effect on pain interference and long-term effect on return to work. The following "stepped-care" approach to pain management that involves psychological intervention has been suggested:

Step 1: Identify and address specific concerns about pain and enhance interventions that emphasize self-management. The role of the psychologist at this point includes education and training of pain care providers in how to screen for patients that may need early psychological intervention.

Step 2: Identify patients who continue to experience pain and disability after the usual time of recovery. At this point a consultation with a psychologist allows for screening, assessment of goals, and further treatment options, including brief individual or group therapy.

Step 3: Pain is sustained in spite of continued therapy (including the above psychological care). Intensive care may be required from mental health professions allowing for a multidisciplinary treatment approach. See also Multi-disciplinary pain programs. (Otis, 2006) (Townsend, 2006) (Kerns, 2005) (Flor, 1992) (Morley, 1999) (Ostelo, 2005)

## **Pulsed radiofrequency treatment (PRF)**

Not recommended. Pulsed radiofrequency treatment (PRF) has been investigated as a potentially less harmful alternative to radiofrequency (RF) thermal neurolytic destruction (thermocoagulation) in the management of certain chronic pain syndromes such as facet joint pain and trigeminal neuralgia. Pulsed radiofrequency treatment is considered investigational/not medically necessary for the treatment of chronic pain syndromes. (BlueCross, 2005) A decrease in pain was observed in patients with herniated disc and spinal stenosis, but not in those with failed back surgery syndrome. However, this option does not appear to be an ideal modality of treatment for lumbar radicular pain because neurodestructive methods for the treatment of neuropathic pain are in principle generally considered inappropriate. (Abejón, 2007)

## **Pumps, implantable**

See Implantable drug-delivery systems (IDDSs).

## **Pycnogenol (maritime pine bark) [DWC]**

Pycnogenol (maritime pine bark) is not recommended for chronic pain.

## **Rapid detox**

Not recommended. Gradual weaning is recommended for long-term opioid users because opioids cannot be abruptly discontinued without probable risk of withdrawal symptoms. The data supporting the safety and effectiveness of opioid antagonist agent detoxification under sedation

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or general anesthesia is limited, and adequate safety has not been established. Given that the adverse events are potentially life threatening, the value of antagonist-induced withdrawal under heavy sedation or anesthesia is not supported. The high cost of anesthesia-based approaches, both in monetary terms and use of scarce intensive care resources, suggest that this form of treatment should not be pursued. (McCabe, 2000) (Gowing-Cochrane, 2006) The American Society of Addiction Medicine (ASAM) issued a revised public policy statement (2005) regarding rapid and ultra-rapid opioid detoxification. The policy recommendations state that opioid detoxification should be part of an integrated continuum of services that promotes ongoing recovery from addiction. Additional policy recommendations state that ultra-rapid detoxification is a procedure with uncertain risks and benefits, and its use in the clinical setting is not supported. (ASAM, 2005) This treatment is not generally covered in the group health arena. (Aetna, 2006) (Blue Cross/Blue Shield, 2006) (CIGNA, 2006)

## **Return to work**

Recommended. Expedited return-to-work has been shown to be more useful in improving function and decreasing pain than extended disability. (Bernacki, 2000) (Boseman, 2001) (Colorado, 2002) (Melhorn, 2000) Lost productive time from common pain conditions among active workers costs an estimated 61.2 billion dollars per year. The majority (76.6%) of the lost productive time was explained by reduced performance while at work and not work absence. (Stewart, 2003) Chronic pain is independently related to low self-rated health in the general population. (Mantyselka-JAMA, 2003) Significant pain improvement is seen in groups that are prescribed light activity over groups that receive only medical treatment, especially in cases involving back pain. Extended bed rest is not recommended. (van Lankveld, 2000)

## **RS-4i sequential stimulator [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **Salicylate topicals [DWC]**

Recommended. Topical salicylate (e.g., Ben-Gay, methyl salicylate) is significantly better than placebo in acute and chronic pain. (Mason-BMJ, 2004) See also Topical analgesics and Topical Analgesics – Compounded [DWC]

## **Sclerotherapy (prolotherapy)**

Not recommended. Sclerotherapy/prolotherapy has no proven value via well-controlled, double blind studies and may have harmful effects. (Chronic Pain, 1998)

## **SNRIs (serotonin noradrenaline reuptake inhibitors)**

See Antidepressants for neuropathic pain. See also venlafaxine (Effexor) and duloxetine (Cymbalta).

## **Spinal cord stimulators (SCS)**

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Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, for specific conditions indicated below, and following a successful temporary trial. Although there is limited evidence in favor of Spinal Cord Stimulators (SCS) for Failed Back Surgery Syndrome (FBSS) and Complex Regional Pain Syndrome (CRPS) Type I, more trials are needed to confirm whether SCS is an effective treatment for certain types of chronic pain. (Mailis-Gagnon-Cochrane, 2004) (BlueCross BlueShield, 2004) See indications list below. See Complete list of SCS\_References. This supporting evidence is significantly supplemented and enhanced when combined with the individually based observational evidence gained through an individual trial prior to implant. This individually based observational evidence should be used to demonstrate effectiveness and to determine appropriate subsequent treatment. (Sundaraj, 2005) Spinal Cord Stimulation is a treatment that has been used for more than 30 years, but only in the past five years has it met with widespread acceptance and recognition by the medical community. In the first decade after its introduction, SCS was extensively practiced and applied to a wide spectrum of pain diagnoses, probably indiscriminately. The results at follow-up were poor and the method soon fell in disrepute. In the last decade there has been growing awareness that SCS is a reasonably effective therapy for many patients suffering from neuropathic pain for which there is no alternative therapy. There are several reasons for this development, the principal one being that the indications have been more clearly identified. The enhanced design of electrodes, leads, and receivers/stimulators has substantially decreased the incidence of re-operations for device failure. Further, the introduction of the percutaneous electrode implantation has enabled trial stimulation, which is now commonly recognized as an indispensable step in assessing whether the treatment is appropriate for individual patients. (Furlan-Cochrane, 2004) These implantable devices have a very high initial cost relative to conventional medical management (CMM); however, over the lifetime of the carefully selected patient, SCS may lead to cost-saving and more health gain relative to CMM for FBSS and CRPS. (Taylor, 2005) (Taylor, 2006) SCS for treatment of chronic nonmalignant pain, including FBSS, has demonstrated a 74% long-term success rate (Kumar, 2006). SCS for treatment of FBSS reported better effectiveness compared to reoperation (North, 2005). CRPS patients implanted with SCS reported pain relief of at least 50% over a median follow-up period of 33 months. SCS appears to be an effective therapy in the management of patients with CRPS. (Kemler, 2000) Permanent pain relief in CRPS-I can be attained under long-term SCS therapy combined with physical therapy. (Harke, 2005) Neuromodulation may be successfully applied in the treatment of visceral pain, a common form of pain when internal organs are damaged or injured, if more traditional analgesic treatments have been unsuccessful. (Kapural, 2006) (Prager, 2007) A recent RCT of 100 failed back surgery syndrome patients randomized to receive spinal cord stimulation plus conventional medical management (SCS group) or conventional medical management alone (CMM group), found that 48% of SCS patients versus 9% of CMM patients achieved the primary outcome of 50% or more pain relief at 6 months. (Kumar, 2007) According to the European Federation of Neurological Societies (EFNS), spinal cord stimulation (SCS) is efficacious in failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) type I (level B recommendation). (Cruccu, 2007) See also Psychological evaluations (SCS) in the Stress & Other Mental Conditions Chapter.

Indications for stimulator implantation:

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- Failed back syndrome (persistent pain in patients who have undergone at least one previous back operation), more helpful for lower extremity than low back pain, although both stand to benefit, 40-60% success rate 5 years after surgery. It works best for neuropathic pain. Neurostimulation is generally considered to be ineffective in treating nociceptive pain. The procedure should be employed with more caution in the cervical region than in the thoracic or lumbar.
- Complex Regional Pain Syndrome (CRPS)/Reflex sympathetic dystrophy (RSD), 70-90% success rate, at 14 to 41 months after surgery. (Note: This is a controversial diagnosis.)
- Post amputation pain (phantom limb pain), 68% success rate
- Post herpetic neuralgia, 90% success rate
- Spinal cord injury dysesthesias (pain in lower extremities associated with spinal cord injury)
- Pain associated with multiple sclerosis
- Peripheral vascular disease (insufficient blood flow to the lower extremity, causing pain and placing it at risk for amputation), 80% success at avoiding the need for amputation when the initial implant trial was successful. The data is also very strong for angina.

### **Spinal cord stimulators, psychological evaluations**

See Psychological evaluations, SCS (spinal cord stimulators).

### **SSRIs (selective serotonin reuptake inhibitors)**

See Antidepressants for neuropathic pain and Antidepressants for non-neuropathic pain.

### **Stellate ganglion block**

Recommended as indicated below. For diagnosis and treatment of sympathetic pain involving the face, head, neck, and upper extremities secondary to CRPS-I and II, and shingles. This block is commonly used for differential diagnosis and is the preferred treatment of CRPS-I pain involving the upper extremity. For diagnostic testing, one should be sufficient. For a positive response, pain relief should be 50% or greater for the duration of the local anesthetic and pain relief should be associated with functional improvement. One to three blocks may be given therapeutically as an adjunct to functional exercise. (Colorado, 2002) (Price, 1998)

### **Substance abuse (tolerance, dependence, addiction)**

The American Pain Society, American Academy of Pain Medicine, and American Society of Addiction Medicine have jointly defined the following (AAPM3, 2001):

1) Tolerance: “A state of adaptation in which exposure to a drug induces changes that result in diminution of one or more of the drug’s effects over time.” This is characterized by the need for higher doses of the medication to achieve the same pain effect and/or a diminished pain relief effect with continued use of the medication. In terms of opioids, most patients develop their plateau dose of opioids within about 2 months. (VA/DoD, 2003) One option to consider besides increasing the dose is to switch to another opioid.

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2) Physical dependence: “A state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.” Abrupt cessation causes physiologic withdrawal. This can be expected with the use of opioids. This is not synonymous with addiction. Tolerance and withdrawal are 2 different conditions.

3) Addiction: “A primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations.”

DSM-IV Criteria for substance dependence (a more serious condition than substance abuse):

1) Tolerance, 2) Withdrawal, 3) The substance is taken in amounts that are greater than intended or for a longer duration, 4) The patient is unable to cut down or quit the substance and/or desires to cut down or quit, 5) A great deal of time is spent obtaining the substance (for example, going to multiple doctors), and a great deal of time is spent in recovering from the effects of the substance, 6) Functioning is affected, including social, occupational and recreational activities, 7) The substance is causing physical or psychological problems and the patient is aware of this, but use is continued. (APA, 1994)

DSM-IV Criteria for substance abuse

1) Failure to fulfill major role obligations at work, school or home, 2) Recurrent substance abuse in situations in which it is physically hazardous, 3) Recurrent legal problems associated with substance abuse, 4) Continued use despite persistent or recurrent social or interpersonal problems related to use.

Red flags for patients that may potentially abuse opioids:

(a) History of alcohol or substance abuse, (b) Active alcohol or substance abuse, (c) Borderline personality disorder, (d) Mood disorders (depression) or psychotic disorders, (e) Non-return to work for >6 months, (f) Poor response to opioids in the past (Washington, 2002)

Red flags of addiction:

1) Adverse consequences: (a) Decreased functioning, (b) Observed intoxication, (c) Negative affective state

2) Impaired control over medication use: (a) Failure to bring in unused medications, (b) Dose escalation without approval of the prescribing doctor, (c) Requests for early prescription refills, (d) Reports of lost or stolen prescriptions, (e) Unscheduled clinic appointments in “distress”, (f) Frequent visits to the ED, (g) Family reports of overuse or intoxication

3) Craving and preoccupation: (a) Non-compliance with other treatment modalities, (b) Failure to keep appointments, (c) No interest in rehabilitation, only in symptom control, (d) No relief of pain or improved function with opioid therapy, (e) Medications are provided by multiple providers. (Wisconsin, 2004)

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## **Sympathectomy**

See CRPS, symathectomy.

## **Sympathetic therapy [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **TENS (Transcutaneous electrical nerve stimulation) [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **TENS, post operative pain (transcutaneous electrical nerve stimulation) [DWC]**

See Transcutaneous Electrotherapy [DWC]

## **Testosterone replacement for hypogonadism (related to opioids) [DWC]**

Recommended in limited circumstances for patients taking high-dose long-term opioids with documented low testosterone levels. Hypogonadism has been noted in patients receiving intrathecal opioids and long term high dose opioids. Routine testing of testosterone levels in men taking opioids is not recommended. However, an endocrine evaluation and/or testosterone levels should be considered in men who are taking long term, high dose oral opioids or intrathecal opioids and who exhibit symptoms or signs of hypogonadism, such as gynecomastia. If needed, testosterone replacement should be done by a physician with special knowledge in this field given the potential side effects such as hepatomas. There are multiple delivery mechanisms for testosterone Hypogonadism secondary to opiates appears to be central, although the exact mechanism has not been determined.

## **THC (tetrahydrocannabinol)**

See **Cannabinoids**.

## **Tiagabine (Gabitril®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Tiagabine listing.

## **Topical Analgesics**

Recommended as an option as indicated below. Largely experimental in use with few randomized controlled trials to determine efficacy or safety. Primarily recommended for neuropathic pain when trials of antidepressants and anticonvulsants have failed. (Namaka, 2004) These agents are applied locally to painful areas with advantages that include lack of systemic side effects, absence of drug interactions, and no need to titrate. (Colombo, 2006) Many agents are compounded as monotherapy or in combination for pain control (including NSAIDs, opioids,

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capsaicin, local anesthetics, antidepressants, glutamate receptor antagonists,  $\alpha$ -adrenergic receptor agonist, adenosine, cannabinoids, cholinergic receptor agonists,  $\gamma$  agonists, prostanoids, bradykinin, adenosine triphosphate, biogenic amines, and nerve growth factor). (Argoff, 2006) There is little to no research to support the use of many these agents. The use of these compounded agents requires knowledge of the specific analgesic effect of each agent and how it will be useful for the specific therapeutic goal required.

### Neuropathic pain.

Lidocaine: Recommended for localized peripheral pain after there has been evidence of a trial of first-line therapy (tri-cyclic or SNRI anti-depressants or an AED such as gabapentin or Lyrica). This is not a first-line treatment and is only FDA approved for post-herpetic neuralgia. Further research is needed to recommend this treatment for chronic neuropathic pain disorders other than post-herpetic neuralgia.. Formulations that do not involve a dermal-patch system are generally indicated as local anesthetics and anti-pruritics. (Argoff, 2006) (Dworkin, 2007) (Khaliq, 2007) (Knotkova, 2007)

Capsaicin: Recommended only as an option in patients who have not responded or are intolerant to other treatments. See also Capsaicin.

Other agents: Topical ketamine has only been studied for use in non-controlled studies for CRPS I and post-herpetic neuralgia, and both studies showed encouraging results. Topical clonidine has published reports in animal studies only. Topical gabapentin has no published reports.

### Non-neuropathic pain (soft tissue injury and osteoarthritis).

NSAIDs: The efficacy in clinical trials for this treatment modality have been inconsistent and most studies are small and of short duration. Topical NSAIDs have been shown in meta-analysis to be superior to placebo during the first 2 weeks of treatment for osteoarthritis, but either not afterward, or with a diminishing effect over another 2-week period. (Lin, 2004) (Bjordal, 2007) (Mason, 2004) When investigated specifically for osteoarthritis of the knee, topical NSAIDs have been shown to be superior to placebo for 4 to 12 weeks. In this study the effect appeared to diminish over time and it was stated that further research was required to determine if results were similar for all preparations. (Biswal, 2006) These medications may be useful for chronic musculoskeletal pain, but there are no long-term studies of their effectiveness or safety. Ketoprofen is under study in a patch formulation for treatment of ankle strain and for tendonitis/bursitis of the elbow, shoulder and knee in phase II clinical trials in Europe.

Capsaicin: Recommended only as an option in patients who have not responded or are intolerant to other treatments. See also Capsaicin.

Lidocaine: There are no randomized controlled trials evaluating the use of topical lidocaine for treatment of low back pain or osteoarthritis, and treatment with this modality is not currently recommended.

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Other agents: Topical glucosamine, chondroitin and camphor showed significant pain relief for osteoarthritis of the knee after 8 weeks compared to placebo. (Cohen, 2003) See also Glucosamine (and Chondroitin Sulfate). For non-neuropathic low back and myofascial pain there are few published studies. (Argoff, 2006)

### **Topical Analgesics – Compounded [DWC]**

Not recommended. There is no evidence that compounding topical medications, such as adding an anti-inflammatory agent to capsaicin, is more efficacious than the single medication. Furthermore, the FDA has issued warnings on the potential dangers of compounding topical medication containing local anesthetics. Exposure to high concentrations of local anesthetics, like those in compounded topical anesthetic creams, can cause grave reactions including seizures and irregular heartbeats. At least two deaths have been connected to compounded topical anesthetic creams. (FDA Advisory 12/05/06)

### **Topiramate (Topamax®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Topiramate listing.

### **Tramadol (Ultram®)**

Tramadol (Ultram®) is a centrally acting synthetic opioid analgesic. See Opioids. See also Diabetic neuropathy; Opioids for neuropathic pain; & Medications for acute pain (analgesics).

### **Transcutaneous Electrotherapy [DWC]**

Electrotherapy represents the therapeutic use of electricity and is another modality that can be used in the treatment of pain. Transcutaneous electrotherapy is the most common form electrotherapy where electrical stimulation is applied to the surface of the skin. The earliest devices were referred to as TENS (transcutaneous electrical nerve stimulation) and are the most commonly used. It should be noted that there is not one fixed electrical specification that is standard for TENS; rather there are several electrical specifications. Other devices (such as H-wave stimulation (devices), Interferential Current Stimulation, Microcurrent electrical stimulation (MENS devices), RS-4i sequential stimulator, Electroceutical Therapy (bioelectric nerve block), Neuromuscular electrical stimulation (NMES devices), Sympathetic therapy, Dynatron STS) have been designed and are distinguished from TENS based on their electrical specifications to be discussed in detail below. The following individual treatment topics are grouped together under the topic heading, “Transcutaneous Electrotherapy [DWC]” and are intended to allow the users of the chronic pain medical treatment guidelines to compare their benefits and to choose amongst the various transcutaneous electrical stimulation devices.

### **TENS, chronic pain (transcutaneous electrical nerve stimulation) [ODG]**

Not recommended as a primary treatment modality, but a one-month home-based TENS trial may be considered as a noninvasive conservative option, if used as an adjunct to a program of evidence-based functional restoration, for the conditions described below.

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While TENS may reflect the long-standing accepted standard of care within many medical communities, the results of studies are inconclusive; the published trials do not provide information on the stimulation parameters which are most likely to provide optimum pain relief, nor do they answer questions about long-term effectiveness. (Carroll-Cochrane, 2001) Several published evidence-based assessments of transcutaneous electrical nerve stimulation (TENS) have found that evidence is lacking concerning effectiveness. One problem with current studies is that many only evaluated single-dose treatment, which may not reflect the use of this modality in a clinical setting. Other problems include statistical methodology, small sample size, influence of placebo effect, and difficulty comparing the different outcomes that were measured.

Recommendations by types of pain: A home-based treatment trial of one month may be appropriate for neuropathic pain and CRPS II (conditions that have limited published evidence for the use of TENS as noted below), and for CRPS I (with basically no literature to support use).

Neuropathic pain: Some evidence (Chong, 2003), including diabetic neuropathy (Spruce, 2002) and post-herpetic neuralgia. (Niv, 2005)

Phantom limb pain and CRPS II: Some evidence to support use. (Finsen, 1988) (Lundeberg, 1985)

Spasticity: TENS may be a supplement to medical treatment in the management of spasticity in spinal cord injury. (Aydin, 2005)

Multiple sclerosis (MS): While TENS does not appear to be effective in reducing spasticity in MS patients it may be useful in treating MS patients with pain and muscle spasm. (Miller, 2007)

How it works: TENS consists of an electrical pulse generator connected to skin-surface electrodes that apply stimulation to peripheral nerves at well-tolerated frequencies. Electrodes can either be placed at the site of pain or other locations, using a trial and error methodology. A TENS unit can be varied by amplitude, pulse width (duration) and pulse rate (frequency). The most common applications include (1) high frequency or conventional TENS (40-150 Hz, with a short duration of up to 50 microseconds) and (2) low frequency or acupuncture-like TENS (1-4 Hz at a high stimulus intensity). Other modes of TENS include: (1) brief-intense TENS (>80 Hz); (2) burst TENS (bursts at less than 10 Hz) at high frequency; and (3) modulation TENS. The difference between clinical effectiveness of the modalities has not been well defined. (Koke, 2004)

Recent studies: There has been a recent meta-analysis published that came to a conclusion that there was a significant decrease in pain when electrical nerve stimulation (ENS) of most types was applied to any anatomic location of chronic musculoskeletal pain (back, knee, hip, neck) for any length of treatment. Of the 38 studies used in the analysis, 35 favored ENS over placebo. All locations of pain were included based on the rationale that “mechanism, rather than anatomic location of pain, is likely to be a critical

## CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

factor for therapy.” The overall design of this study used questionable methodology and the results require further evaluation before application to specific clinical practice. (Johnson, 2007) (Novak, 2007) (Furlan, 2007)

Current Treatment Coverage Guidelines:

- BlueCross BlueShield: TENS is considered investigational for treatment of chronic back pain, chronic pain and post-surgical pain, but is covered for certain members based on CMS rules. (BlueCross BlueShield, 2007)
- CMS: The use of TENS for the relief of acute post-operative pain is covered for 30 days or less (as an adjunct and/or alternative to pharmaceutical treatment). TENS is also covered as treatment for chronic intractable pain. Medicare requires a month-long trial period in order to determine if there is a significant therapeutic effect. (Medicare, 2006)
- Aetna & Humana: consistent with the CMS Guidelines (Aetna, 2005) (Humana, 2004)
- VA: TENS is considered equivocal when compared to other modalities. (US Dept VA, 2001)
- European Federation of Neurological Societies (EFNS): TENS may be better than placebo (level C) although worse than electro-acupuncture (level B); TENS is non-invasive and suitable as a preliminary or add-on therapy. (Cruccu, 2007)

Criteria for the use of TENS:

Chronic intractable pain (for the conditions noted above):

- Documentation of pain of at least three months duration
- There is evidence that other appropriate pain modalities have been tried (including medication) and failed
- A one-month trial period of the TENS unit should be documented (as an adjunct to ongoing treatment modalities within a functional restoration approach) with documentation of how often the unit was used, as well as outcomes in terms of pain relief and function; rental would be preferred over purchase during this trial
- Other ongoing pain treatment should also be documented during the trial period including medication usage
- A treatment plan including the specific short- and long-term goals of treatment with the TENS unit should be submitted
- A 2-lead unit is generally recommended; if a 4-lead unit is recommended, there must be documentation of why this is necessary

Form-fitting TENS device: This is only considered medically necessary when there is documentation that there is such a large area that requires stimulation that a conventional system cannot accommodate the treatment, that the patient has medical conditions (such as skin pathology) that prevents the use of the traditional system, or the TENS unit is to be used under a cast (as in treatment for disuse atrophy)

# CHRONIC PAIN MEDICAL TREATMENT GUIDELINES

## **TENS, post operative pain (transcutaneous electrical nerve stimulation) [ODG]**

Recommended as a treatment option for acute post-operative pain in the first 30 days post-surgery. Transcutaneous electrical nerve stimulation (TENS) appears to be most effective for mild to moderate thoracotomy pain. (Solak, 2007) (Erdogan, 2005). It has been shown to be of lesser effect, or not at all for other orthopedic surgical procedures. (Breit, 2004) (Rosenquist 2003) The proposed necessity of the unit should be documented upon request. Rental would be preferred over purchase during this 30-day period.

## **H-wave stimulation (devices) [ODG]**

Not recommended as an isolated intervention, but a one-month home-based trial of H-Wave stimulation may be considered as a noninvasive conservative option for diabetic neuropathic pain, if used as an adjunct to a program of evidence-based functional restoration, and only following failure of other recommended pain modalities. There is no evidence that H-Wave is more effective than TENS despite the significantly higher cost of H-Wave, so TENS would be recommended for the treatment of diabetic neuropathy over H-Wave unless documentation can support medical necessity. While H-Wave and other similar type devices can be useful for pain management, they are often over-prescribed and used as a passive intervention rather than as a tool in combination with functional restoration. For diabetic neuropathy unresponsive to more conventional treatment, a one-month trial may be appropriate to permit the physician and physical therapist to study the effects and benefits, and it should be documented (as an adjunct to ongoing treatment modalities within a functional restoration approach) with documentation of how often the unit was used, as well as outcomes in terms of pain relief and function; rental would be preferred over purchase during this trial. Trial periods of more than one month should be justified by documentation submitted for review. Three small controlled trials provide suggestive evidence about the effectiveness of H-wave electrical stimulation for diabetic neuropathy, but evidence is lacking for other conditions. There are no high quality studies demonstrating the effectiveness of H-Wave for conditions other than diabetic neuropathy. H-wave stimulation is a form of electrical stimulation that differs from other forms of electrical stimulation, such as transcutaneous electrical nerve stimulation (TENS), in terms of its waveform. While physiatrists, chiropractors, or podiatrists may perform H-wave stimulation, H-wave devices are also available for home use. H-wave stimulation is sometimes used for the treatment of pain related to a variety of etiologies, muscle sprains, temporomandibular joint dysfunctions or reflex sympathetic dystrophy. In fact, H-wave is used more often for muscle spasm and acute pain as opposed to neuropathy or radicular pain, since there is anecdotal evidence that H-Wave stimulation helps to relax the muscles, but there are no published studies to support this use, so it is not recommended. H-wave stimulation has also been used to accelerate healing of wounds, such as diabetic ulcers. H-wave electrical stimulation must be distinguished from the H-waves that are a component of electromyography. (Julka, 1998) (Kumar, 1997) (Kumar, 1998) (McDowell, 1999)

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(McDowell<sup>2</sup>, 1999) (BlueCross BlueShield, 2005) (Aetna, 2005) (Blum, 2006) (Blum<sup>2</sup>, 2006)

## **Interferential Current Stimulation [ODG]**

Not generally recommended. The randomized trials that have evaluated the effectiveness of this treatment have included studies for back pain, jaw pain, soft tissue shoulder pain, cervical neck pain and post-operative knee pain. (Van der Heijden, 1999) (Werner, 1999) (Hurley, 2001) (Hou, 2002) (Jarit, 2003) (Hurley, 2004) (CTAF, 2005) The findings from these trials were either negative or non-interpretable for recommendation due to poor study design and/or methodologic issues. In addition, although proposed for treatment in general for soft tissue injury or for enhancing wound or fracture healing, there is insufficient literature to support Interferential current stimulation for treatment of these conditions. There are no standardized protocols for the use of interferential therapy; and the therapy may vary according to the frequency of stimulation, the pulse duration, treatment time, and electrode-placement technique.

How it works: Paired electrodes of two independent circuits carry differing medium-frequency alternating currents so that current flowing between each pair intersects at the underlying target. The frequency allows the Interferential wave to meet low impedance when crossing the skin. Treatments involve the use of two pairs of electrodes and most units allow variation in waveform, stimulus frequency and amplitude or intensity, and the currents rise and fall at different frequencies. It is theorized that the low frequency of the interferential current causes inhibition or habituation of the nervous system, which results in muscle relaxation, suppression of pain and acceleration of healing.

How it is different than TENS: It has been postulated that Interferential stimulation allows for deeper penetration of tissue, whereas TENS is predominantly a cutaneous or superficial stimulus. Interferential current is proposed to produce less impedance in the tissue and the intensity provided is suggested to be perceived as more comfortable. Because there is minimal skin resistance with the interferential current therapy, a maximum amount of energy goes deeper into the tissue. It also crisscrosses, as opposed to the linear application of the TENS. This crisscrossing is postulated to be more effective because it serves to confuse the nerve endings, preventing the treated area from adjusting to the current. There are no published randomized trials comparing TENS to Interferential current stimulation.

Current US treatment coverage recommendations:

California Technology Assessment Forum: The treatment does not meet the CTAF criteria 2-5 for the treatment of musculoskeletal pain. Interferential stimulation did meet the criterion for meeting appropriate regulatory approval. (CTAF, 2005)

Aetna: Considered experimental and investigational for the reduction of pain and edema and all other indications because its effectiveness for these indications has not been established. (Aetna, 2007)

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BlueCross BlueShield: Considered investigational/not medically necessary to provide pain relief associated with soft tissue injury, musculoskeletal disorders, or in enhancing wound and fracture healing. (BlueCross BlueShield, 2006)

CMS: Does not directly address the use of Interferential stimulator treatment. See also Sympathetic therapy. See also TENS, chronic pain.

While not generally recommended, Patient selection criteria if Interferential stimulation is to be used anyway:

Possibly appropriate for the following conditions if it has documented and proven to be effective as applied by a licensed physical therapist:

- Pain is ineffectively controlled due to diminished effectiveness of medications; or
- Pain is ineffectively controlled with medications due to side effects; or
- History of substance abuse; or
- Significant pain from postoperative or acute conditions limits the ability to perform exercise programs/physical therapy treatment; or
- Unresponsive to conservative measures (e.g., repositioning, heat/ice, etc.).

If those criteria are met, then a one-month trial may be appropriate to permit the physician and physical therapist to study the effects and benefits. There should be evidence of increased functional, less reported pain and evidence of medication reduction.

A “jacket” should not be certified until after the one-month trial and only with documentation that the individual cannot apply the stimulation pads alone or with the help of another available person.

### **Microcurrent electrical stimulation (MENS devices) [ODG]**

Not recommended. Based on the available evidence conclusions cannot be made concerning the effect of Microcurrent Stimulation Devices (MENS) on pain management and objective health outcomes. MENS is characterized by sub-sensory current that acts on the body's naturally occurring electrical impulses to decrease pain and facilitate the healing process. MENS differs from TENS in that it uses a significantly reduced electrical stimulation. TENS blocks pain, while MENS acts on the naturally occurring electrical impulses to decrease pain by stimulating the healing process. (BlueCross BlueShield, 2005)

### **RS-4i sequential stimulator [ODG]**

**See Interferential current stimulation (ICS).**

### **Electroceutical Therapy (bioelectric nerve block) [ODG]**

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Not recommended. Electroceutical therapy (also known as bioelectric nerve block) is experimental and investigational for the treatment of acute pain or chronic pain (e.g., back pain, diabetic pain, joint pain, fibromyalgia, headache, and CRPS) because there is a lack of scientific evidence regarding the effectiveness of this technology. In addition, electroceutical treatments use much higher electrical frequencies than TENS units and may only be prescribed and administered under the supervision of a healthcare provider experienced in this method of treatment. (Aetna, 2005)

### **Neuromuscular electrical stimulation (NMES devices) [DWC]**

Not recommended. NMES is used primarily as part of a rehabilitation program following stroke and there is no evidence to support its use in chronic pain.

### **Sympathetic therapy [ODG]**

Not recommended. Sympathetic therapy is considered investigational. The lack of published outcomes from well-designed clinical trials prohibits scientific conclusions concerning the health outcome effects of sympathetic therapy for the treatment of pain. Sympathetic therapy describes a type of electrical stimulation of the peripheral nerves that is designed to stimulate the sympathetic nervous system in an effort to "normalize" the autonomic nervous system and alleviate chronic pain. Unlike TENS (transcutaneous electrical nerve stimulation) or interferential electrical stimulation, sympathetic therapy is not designed to treat local pain, but is designed to induce a systemic effect on sympathetically induced pain. The Dynatron STS device and a companion home device, Dynatron STS Rx, are devices that deliver sympathetic therapy. These devices received U.S. Food and Drug Administration (FDA) clearance in March 2001 through a 510(k) process. The FDA-labeled indication is as follows: "Electrical stimulation delivered by the Dynatron STS and Dynatron STS Rx is indicated for providing symptomatic relief of chronic intractable pain and/or management of post-traumatic or post-surgical pain." (Werners, 1999) (Washington, 2002) (BlueCross Blue-shield, 2005) (Aetna, 2005)

### **Dynatron STS [ODG]**

See Sympathetic therapy.

### **Treatment for CRPS**

See CRPS, treatment

### **Trigger point injections**

Recommended only for myofascial pain syndrome as indicated below, with limited lasting value. See Myofascial pain. Not recommended for radicular pain. A trigger point is a discrete focal tenderness located in a palpable taut band of skeletal muscle, which produces a local twitch in response to stimulus to the band. Myofascial pain syndrome is a regional painful muscle condition with a direct relationship between a specific trigger point and its associated pain

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region. These injections may occasionally be necessary to maintain function in those with myofascial problems when myofascial trigger points are present on examination. Not recommended for typical back pain or neck pain. (Graff-Radford, 2004) (Nelemans-Cochrane, 2002) See also the Low Back Chapter. For fibromyalgia syndrome, trigger point injections have not been proven effective. (Goldenberg, 2004)

Criteria for the use of Trigger point injections:

Trigger point injections with a local anesthetic with or without steroid may be recommended for the treatment of chronic low back or neck pain with myofascial pain syndrome when all of the following criteria are met: (1) Documentation of circumscribed trigger points with evidence upon palpation of a twitch response as well as referred pain; (2) Symptoms have persisted for more than three months; (3) Medical management therapies such as ongoing stretching exercises, physical therapy, NSAIDs and muscle relaxants have failed to control pain; (4) Radiculopathy is not present (by exam, imaging, or neuro-testing); (5) Not more than 4 injections per session; (6) No repeat injections unless a greater than 50% pain relief is obtained for six weeks after an injection and there is documented evidence of functional improvement; (7) Frequency should not be at an interval less than two months; (8) Trigger point injections with any substance (e.g., saline or glucose) other than local anesthetic with or without steroid are not recommended. (Colorado, 2002) (BlueCross BlueShield, 2004)

### **Turmeric**

See Curcumin (Turmeric).

### **Ultrasound, therapeutic**

Not recommended. Therapeutic ultrasound is one of the most widely and frequently used electrophysical agents. Despite over 60 years of clinical use, the effectiveness of ultrasound for treating people with pain, musculoskeletal injuries, and soft tissue lesions remains questionable. There is little evidence that active therapeutic ultrasound is more effective than placebo ultrasound for treating people with pain or a range of musculoskeletal injuries or for promoting soft tissue healing. (Robertson, 2001)

### **Uncaria Tomentosa (Cat's Claw) [DWC]**

Uncaria Tomentosa (Cat's Claw) is not recommended for chronic pain.

### **Venlafaxine (Effexor®)**

Recommended as an option in first-line treatment of neuropathic pain. Venlafaxine (Effexor®) is a member of the selective-serotonin reuptake inhibitor class of antidepressants. It has FDA approval for treatment of depression and anxiety disorders. It is off-label recommended for treatment of neuropathic pain, diabetic neuropathy, fibromyalgia, and headaches. The initial dose is generally 37.5 to 75 mg/day with a usual increase to a dose of 75 mg b.i.d or 150 mg/day of the ER formula. The maximum dose of the immediate release formulation is 375 mg/day and

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of the ER formula is 225 mg/day. It may have an advantage over tricyclic antidepressants due to lack of anticholinergic side effects. Dosage requirements are necessary in patients with hepatic and renal impairment. (Namaka, 2004) See also Antidepressants for neuropathic pain.

### **Vicodin®**

See Opioids

### **Vioxx® (rofecoxib)**

Not recommended. Note: Pulled from market 10/5/04. See Anti-inflammatory medications and NSAIDs (non-steroidal anti-inflammatory drugs). Recent studies have shown an increase in the risk of myocardial infarction for rofecoxib (Vioxx), compared to NSAID's with an antiplatelet effect. (Choi, 2004) (Solomon, 2004)

### **Weaning of Medications**

Recommended as indicated below. For opioids a slow taper is recommended. The longer the patient has taken opioids, the more difficult they are to taper. The process is more complicated with medical comorbidity, older age, female gender, and the use of multiple agents. Gradual weaning is recommended for long-term opioid users because opioids cannot be abruptly discontinued without probable risk of withdrawal symptoms. (Benzon, 2005) Patients with complex conditions with multiple comorbidities (including psych disorders) should be referred to an addiction medicine/psychiatry specialist. Opioid weaning should include the following: (a) Start with a complete evaluation of treatment, comorbidity, psychological condition, (b) Clear written instructions should be given to the patient and family, (c) If the patient can not tolerate the taper, refer to an expert (pain specialist, substance abuse specialist), (d) Taper by 20 to 50% per week of original dose for patients who are not addicted (the patient needs 20% of the previous day's dose to prevent withdrawal), (e) Greater success may occur when the patient is switched to longer-acting opioids and then tapered, (f) Office visits should occur on a weekly basis, (g) Assess for withdrawal using a scale such as the Subjective Opioid Withdrawal Scale (SOWS) and Objective Opioid Withdrawal Scale (OOWS), and (h) Recognize that this may take months. For benzodiazepines, tapering is required if used for greater than 2 weeks. (Benzon, 2005) (Ashton, 2005) This is more dangerous than opioid withdrawal, and takes more time, with the following recommendations: (1) The recommended rate of tapering is about 1/8 to 1/10 of the daily dose every 1 to 2 weeks, (2) Rate of withdrawal should be individually tapered, (3) Tapering may take as long as a year, (4) High-dose abusers or those with polydrug abuse may need in-patient detoxification, and (5) Withdrawal can occur when a chronic user switches to a benzodiazepine with a different receptor activity. (Lee, 2002) For carisoprodol (Soma®), this medication is metabolized to meprobamate, a barbiturate. At the highest levels of barbiturate tolerance, the patient is at risk of delirium, seizures or even death with abrupt discontinuation. (Heacock, 2004) (Washington, 2002) See also Detoxification; & Rapid detox.

### **White willow bark [DWC]**

White willow bark is not recommended for chronic pain.

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## Yoga

Recommended as an option only for select, highly motivated patients. There is considerable evidence of efficacy for mind-body therapies such as yoga in the treatment of chronic pain. Also, the impact on depression and disability could be considered as important outcomes for further study. Since outcomes from this therapy are very dependent on a highly motivated patient, we recommend approval where requested by a specific patient, but not adoption for use by any patient. (Astin, 2003) (Barrows, 2002) (Galantino, 2004)

## Ziconotide (Prialt®)

Recommended for use after there is evidence of a failure of a trial of intrathecal morphine and dilaudid, and only in individuals for whom the potential benefits outweigh the risks of serious neuropsychiatric adverse effects. The 2007 Polyanalgesic Consensus Conference Recommendations for the Management of Pain by Intrathecal Drug Delivery concluded that ziconotide should be updated to a first-line intrathecal drug.

Ziconotide (Prialt®) is a synthetic calcium channel blocker that is delivered intrathecally, offering a non-opioid option for treatment of chronic pain, and possibly, spasticity associated with spinal cord trauma. It is FDA-approved for the management of severe chronic pain in patients for whom intrathecal therapy is warranted and who are intolerant of other treatments, such as systemic analgesics, adjunctive therapies, or other first-line treatment. This medication is meant to be an option for patients who are intolerant and/or refractory to intrathecal morphine. The advantage of the medication is that it is considered non-addictive. Current case reports have described many challenges in converting from morphine to ziconotide, including inadequate analgesia, adverse medication effects, and opioid withdrawal symptoms. An option for treatment is combining ziconotide with other currently available intrathecal medications, although this has not been studied in placebo-controlled trials.

Adverse effects: Prialt has been associated with severe CNS-related adverse effects, and a “black-box” warning has been issued in this regard. Neurological warnings include hallucinations, paranoid ideation, hostility, delirium, psychosis, manic reactions and decreased alertness. Certain patients may be at increased risk for psychiatric side effects including those with pre-existing history of depression with risk of suicide and patients with pre-existing psychosis. Cognitive impairment was noted in approximately 30% of patients in clinical trials, and this symptom was found to be reversible within about two weeks of discontinuation. Prialt is contraindicated in patients with a pre-existing history of psychosis. Prialt can be discontinued abruptly without evidence of withdrawal effects in the presence of serious adverse events.

Dosage requirements: The current recommendations suggested by the manufacturer for this medication include a low initial infusion rate (0.1 mcg/hour for a total of 2.4 mcg/day) and limiting infusion increases to 2-3 times a week. Current drug trials have evaluated the efficacy of the medication for a 3-week duration only, but preliminary trials suggested that analgesic efficacy would be maintained long-term in open label trials.

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Post-marketing dose recommendations: Post-marketing, an expert consensus-panel recommended a starting dose of 0.5 mcg/24 hours with upward titration of no more than 0.5 mcg/week due to increased risk of adverse effects with higher doses. (Fisher, 2005)

Filling intervals: The reservoir should be refilled initially at 14 days and at 40-day intervals thereafter if the drug is diluted (60 days if undiluted).

Other precautions: This medication is associated with elevation of serum creatinine kinase, with risk factors including male gender and concomitant use of anti-depressants, anti-convulsants and intrathecal morphine. This lab value should be monitored at least bi-weekly for the first month and at monthly intervals thereafter. Symptoms of myalgia include myasthenia, muscle cramps and unusual fatigue. (Thompson, 2006) (Wermeling 2005) (Lyseng-Williamson, 2006) (Lynch, 2006) (Deer, 2007) (Rauck, 2006) See Intrathecal drug delivery systems, medications.

### **Zonisamide (Zonegran®)**

See Anti-epilepsy drugs (AEDs) for general guidelines, as well as specific Zonisamide listing.