



## General

### Guideline Title

Complex regional pain syndrome/reflex sympathetic dystrophy medical treatment guideline.

### Bibliographic Source(s)

Colorado Division of Workers' Compensation. Complex regional pain syndrome/reflex sympathetic dystrophy medical treatment guideline. Denver (CO): Colorado Division of Workers' Compensation; 2017 Nov 30. 96 p.

### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Colorado Division of Workers' Compensation. Complex regional pain syndrome/reflex sympathetic dystrophy: medical treatment guidelines. Denver (CO): Colorado Division of Workers' Compensation; 2011 Dec 27. 107 p.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report [Clinical Practice Guidelines We Can Trust](#).

■■■■■ = Poor   
 ■■■■ = Fair   
 ■■■■ = Good   
 ■■■■■ = Very Good   
 ■■■■■ = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
<span style="color: blue;">■■■■</span>	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition

YES	Multidisciplinary Group
YES	Methodologist Involvement
■■■■□□	Patient and Public Perspectives
	<b>Use of a Systematic Review of Evidence</b>
■■■■□□	Search Strategy
■■■■■	Study Selection
■■■■□	Synthesis of Evidence
	<b>Evidence Foundations for and Rating Strength of Recommendations</b>
■■■■□	Grading the Quality or Strength of Evidence
■■■■■	Benefits and Harms of Recommendations
■■■■□	Evidence Summary Supporting Recommendations
■■■■□□	Rating the Strength of Recommendations
■■■■□	<b>Specific and Unambiguous Articulation of Recommendations</b>
■■■■□	<b>External Review</b>
■■■■■	<b>Updating</b>

## Recommendations

### Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This summary includes the treatment recommendations of the guideline. See the original guideline document for additional information on initial evaluation, overview of care for complex regional pain syndrome (CRPS) or sympathetically mediated pain, and diagnostic criteria and procedures for patients with CRPS/reflex sympathetic dystrophy and for further descriptions of the therapies discussed below.

The grades of recommendations (Some, Good, Strong) are defined at the end of the Major Recommendations field.

#### Therapeutic Procedures—Non-operative

Non-operative therapeutic rehabilitation is applied to patients with CRPS or sympathetically mediated pain (SMP) who experience chronic and complex problems of de-conditioning and functional disability. Treatment modalities may be utilized sequentially or concomitantly depending on chronicity and complexity of the problem, and treatment plans should always be based on a diagnosis utilizing appropriate diagnostic procedures.

Before initiation of any therapeutic procedure, the authorized treating physician, employer and insurer

must consider these important issues in the care of the injured worker:

Patients undergoing therapeutic procedure(s) should be released or returned to modified or restricted duty during their rehabilitation at the earliest appropriate time. Refer to the section "Return-to-Work" below for detailed information.

Reassessment of the patient's status in terms of functional improvement should be documented after each treatment. If patients are not responding within the recommended time periods, alternative treatment interventions, further diagnostic studies, or consultations should be pursued. Continued treatment should be monitored using objective measures such as:

- Return to work or maintaining work status

- Fewer restrictions at work or performing activities of daily living (ADLs)

- Decrease in usage of medications related to the work injury

- Measurable functional gains, such as increased range-of-motion or documented increase in strength

Clinicians should provide and document education to the patient. No treatment plan is complete without addressing issues of individual and/or group patient education as a means of facilitating self-management of symptoms.

Psychological or psychosocial screening should be performed on all chronic pain patients.

### Acupuncture

Acupuncture is recommended for subacute or chronic pain patients who are trying to increase function and/or decrease medication usage and have an expressed interest in this modality. It is also recommended for subacute or acute pain for patients who cannot tolerate nonsteroidal anti-inflammatory drugs (NSAIDs) or other medications, and it should generally be used in conjunction with manipulative and physical therapy/rehabilitation.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for indications, evidence, and time frames.

### Biofeedback

Biofeedback is a form of behavioral medicine that helps patients learn self-awareness and self-regulation skills for the purpose of gaining greater control of their physiology, such as muscle activity, brain waves, and measures of autonomic nervous system activity. Stress-related psycho-physiological reactions may arise as a reaction to organic pain and in some cases may cause pain. Electronic instrumentation is used to monitor the targeted physiology and then displayed or fed back to the patient visually, auditorily, or tactilely, with coaching by a biofeedback specialist.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for indications, evidence, and time frames.

### Complementary Medicine

Complementary medicine, termed complementary alternative medicine (CAM) in some systems, is a term used to describe a broad range of treatment modalities, a number of which are generally accepted and supported by some scientific literature and others which still remain outside the generally accepted practice of conventional Western medicine. In many of these approaches, there is attention given to the relationship between physical, emotional, and spiritual well-being. While CAM may be performed by a myriad of both licensed and non-licensed health practitioners with training in one or more forms of therapy, credentialed practitioners should be used when available or applicable.

All CAM treatments require prior authorization and must include agreed upon number of visits for time to produce functional effects.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for indications, evidence, and time frames.

### Disturbances of Sleep

Disturbances of sleep are common in chronic pain. An essential element of chronic pain treatment is restoration of normal sleep cycles. Although primary insomnia may accompany pain as an independent comorbid condition, it more commonly occurs secondary to the pain condition itself. Exacerbations of pain often are accompanied by exacerbations of insomnia; the reverse can also occur. Sleep laboratory studies have shown disturbances of sleep architecture in pain patients. Loss of deep slow-wave sleep and an increase in light sleep occur. Sleep efficiency, the proportion of time in bed spent asleep, is also decreased. These changes are associated with patient reports of non-restorative sleep. Sleep apnea may also occur as a primary diagnosis or be caused or exacerbated by opioid and hypnotic use.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for more information on behavioral modifications to address sleep disturbances.

#### Education/Informed/Shared Decision Making

##### Evidence Statements Regarding Education/Informed Decision Making

###### Some Evidence

Information provided only by video is not sufficient education (Design: Prospective randomized controlled trial).

See the original guideline document for time to produce effect and frequency.

###### Injections—Therapeutic

For post maximum medical improvement (MMI) care, refer to Section J.4, Maintenance Management, Injection Therapy, in the original guideline document.

###### *Sympathetic Injections*

See the original guideline document for description, indications, special considerations, complications, contraindications, relative contraindications, drugs affecting coagulations, and treatment parameters, as well as time to produce effect, frequency, and optimum and maximum duration of treatments.

###### *Peripheral Nerve Blocks*

These are diagnostic injections that may be used for specific nerve injury or entrapment syndromes. Not all peripheral nerve blocks require fluoroscopy. On occasion they are used for treatment in chronic pain or CRPS. Repeat injection for treatment should be based on functional changes. These injections are usually limited to 3 injections per site per year.

###### *Other Intravenous (IV) Medications and Regional Blocks*

It is unlikely that either type of block provides a significant clinical advantage to the patient; therefore, they are *not recommended*. Intravenous blocks with guanethidine, ketanserin, beryllium phentolamine, reserpine, droperidol and atropine are also *not recommended* due to lack of effect in small studies.

##### Evidence Statement Regarding Other Intravenous Medications and Regional Blocks

###### Some Evidence

There is little advantage of IV regional block with guanethidine over saline blocks with respect to the resolution of tenderness in the affected hand, but the resolution of vasomotor instability may be delayed by guanethidine (Design: Randomized clinical trial).

###### *Continuous Brachial Plexus Infusions*

These infusions are *not recommended* due to possible complications of bleeding, infection, pneumothorax, phrenic nerve paralysis, and lack of literature documenting effectiveness and cost.

###### *Epidural Infusions*

These are *not recommended*.

### Evidence Statements Regarding Epidural Infusions

#### Some Evidence

There is high rate of infection (33%), which can include meningitis (Design: Crossover randomized clinical trial).

#### *Ketamine*

Ketamine is referenced in "Therapeutic Procedures, Non-Operative, CRPS-Specific Medications" in the original guideline document.

#### Interdisciplinary Rehabilitation Programs

##### *Formal Interdisciplinary Rehabilitation Programs*

See the original guideline document for time to produce effect, and optimum and maximum durations, as well as information on occupational rehabilitation, and opioid/chemical treatment programs.

##### *Information Interdisciplinary Rehabilitation Program*

See the original guideline document for time to produce effect, frequency, and optimum and maximum durations.

### Evidence Statements Regarding Interdisciplinary Rehabilitation Programs

#### Good Evidence

Interdisciplinary programs that include screening for psychological issues, identification of fear-avoidance beliefs and treatment barriers, and establishment of individual functional and work goals will improve function and decrease disability (Design: Design: Cluster randomized trial, randomized clinical trial).

Multidisciplinary rehabilitation (physical therapy and either psychological, social, or occupational therapy) shows small effects in reducing pain and improving disability compared to usual care, and multidisciplinary biopsychosocial rehabilitation is more effective than physical treatment for disability improvement after 12 months of treatment in patients with chronic low back pain. Patients with a significant psychosocial impact are most likely to benefit (Design: Meta-analysis of randomized clinical trials).

Exercise alone or as part of a multidisciplinary program results in decreased disability for workers with non-acute low back pain (Design: Meta-analysis of randomized clinical trials).

#### Some Evidence

Telephone-delivered collaborative care management intervention for primary care veteran patients produced clinically meaningful improvements in pain at 12-month follow-up compared with usual care by increasing non-opioid analgesic medications and without changing opioid usage for the management of chronic musculoskeletal pain. The management was directed by nurse case managers. Because the control group was usual care rather than an attention control, the non-specific effects of attention received in the intervention group could have contributed to the effectiveness of the intervention. If an attention control had been used as the control group, the effect size observed for improvement in pain in the intervention group may have been smaller. It is unknown how successful this would be with injured workers (Design: Single-blind randomized clinical trial).

An integrated care program, consisting of workplace interventions and graded activity teaching that pain need not limit activity, is effective in returning patients with chronic low back pain to work, even with minimal reported reduction of pain (Design: Randomized clinical trial).

#### Medications and Medical Management

## *General Chronic Pain Medication Management*

Chronic use of NSAIDs is generally *not recommended* due to increased risk of cardiovascular events and gastrointestinal (GI) bleeding.

### Evidence Statements Regarding Medication Management

#### Some Evidence

In the setting of uncomplicated low back pain lasting longer than 3 months, patients who were willing to participate in a trial of capsules clearly labelled as placebo experienced short-term reductions in pain and disability after the principles of the placebo effect had been explained to them (Design: Randomized clinical trial).

## *CRPS-Specific Medication Management*

### Evidence Statements Regarding CRPS Specific Medication Management

#### Good Evidence

There is little clinical outcome difference between amitriptyline (Elavil, Endep, Vanatrip) and gabapentin or carbamazepine (Carbatrol, Epitol, Equetro, Tegretol), although gabapentin may be better tolerated (Design: Randomized crossover trial, randomized clinical trial, meta-analysis of randomized trials).

The following drug classes are outlined for CRPS-specific neuropathic pain:

Oral steroids

Bisphosphonates

Vitamin C

Ketamine hydrochloride: Due to the potential harm and limited short-term benefit in patients with CRPS, ketamine N-methyl-D-aspartate (NMDA) receptor antagonists are *not recommended* since less harmful therapies are available.

Calcitonin is not approved by the U.S. Food and Drug Administration (FDA) for use with CRPS. Some patients have GI side effects and hyperglycemia has been reported. Rare cases of neurological side effects have been reported. It is *not recommended*.

### Evidence Statements Regarding CRPS-Specific Medications: Oral Steroids

#### Good Evidence

There is good evidence to support oral steroid use early in the course of CRPS (Design: Randomized clinical trials).

### Evidence Statements Regarding CRPS-Specific Medications: Bisphosphonates

#### Good Evidence

Use of bisphosphonates effectively decreases pain (Design: Randomized clinical trial).

#### Some Evidence

Use of bisphosphonates increases joint motion in patients with CRPS (Design: Randomized clinical trial).

### Evidence Statements Regarding CRPS-Specific Medications: Vitamin C

#### Some Evidence

Vitamin C 500 mg to 2 grams taken for 50 days after a wrist fracture may help to prevent CRPS (Design: Randomized clinical trial).

### Evidence Statements Regarding CRPS-Specific Medications: Ketamine Hydrochloride

#### Some Evidence

In CRPS I patients, low dose daily infusions of ketamine can provide pain relief compared to placebo. The relief, however, faded within a few weeks (Design: Randomized clinical trial).

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for a list of drug classes to address neuropathic pain, including evidence and time frames for alpha-acting agents, anticonvulsants, antidepressants, cannabinoid products, hypnotics and sedatives, NSAIDs, post-operative pain management, skeletal muscle relaxants, smoking cessation medications and treatment, topical drug delivery, and other agents.

### *Opioids*

#### Evidence Statements Regarding Effectiveness and Side Effects of Opioids

##### Strong Evidence

In the setting of chronic nonspecific low back pain, the short and intermediate term reduction in pain intensity of opioids, compared with placebo, falls short of a clinically important level of effectiveness (Design: Systematic review and meta-analysis).

Adverse events such as constipation, dizziness, and drowsiness are more frequent with opioids than with placebo (Design: Systematic review and meta-analysis).

##### Good Evidence

Opioids are more efficient than placebo in reducing neuropathic pain by clinically significant amounts (Design: Systematic review and meta-analysis of randomized clinical trials).

Opioids produce significantly more adverse effects than placebo such as constipation, drowsiness, dizziness, nausea, and vomiting (Design: Systematic review and meta-analysis of randomized clinical trials).

Naloxegol can alleviate opioid induced constipation and 12.5 mg starting dose has an acceptable side effect profile (Design: Two identical and simultaneous multicenter randomized double-blind studies).

##### Some Evidence

In the setting of chronic low back pain with disc pathology, a high degree of anxiety or depressive symptomatology is associated with relatively less pain relief in spite of higher opioid dosage than when these symptoms are absent (Design: Prospective cohort study).

#### Evidence Statements Regarding Opioids and Adverse Events

##### Good Evidence

In generally healthy patients with chronic musculoskeletal pain, treatment with long-acting opioids, compared to treatments with anticonvulsants or antidepressants, is associated with an increased risk of death of approximately 69%, most of which arises from non-overdose causes, principally cardiovascular in nature. The excess cardiovascular mortality principally occurs in the first 180 days from starting opioid treatment (Design: Retrospective matched cohort study).

Prescription opioids in excess of 200 morphine milligram equivalents (MME) average daily doses are associated with a near tripling of the risk of opioid-related death, compared to average daily doses of 20 MME. Average daily doses of 100-200 mg and doses of 50-99 mg per day may be associated with a doubling of mortality risk, but these risk estimates need to be replicated with larger studies (Design: Nested case-control study with incidence density sampling).

##### Some Evidence

Compared to an opioid dose under 20 MME per day, a dose of 20-50 mg nearly doubles the risk of death, a dose of 50 to 100 mg may increase the risk more than fourfold, and a dose greater than 100 mg per day may increase the risk as much as sevenfold. However, the absolute risk of fatal overdose of in chronic pain patients is fairly low, and may be as low as 0.04% (Design: Case-cohort study).

Types of opioids are listed below:

Buprenorphine (various formulations) is *not recommended* for most chronic pain patients due to methods of administration, reports of euphoria in some patients, and lack of proof for improved efficacy in comparison with other opioids

Codeine with acetaminophen

Fentanyl (Actiq, Duragesic, Fenora, Sublimaze) is *not recommended* for use with musculoskeletal chronic pain patients.

Meperidine (Demerol) is *not recommended* for chronic pain.

Methadone

Morphine

Oxycodone and hydromorphone

Propoxyphene (Darvon, Davon-N, PP-Cap) has been withdrawn from the market due to cardiac effects including arrhythmias.

Tapentadol (Nucynta)

Tramadol (Rybix, Ryzolt, Ultram)

Primary laboratory monitoring is recommended for acetaminophen/aspirin/NSAIDs combinations (renal and liver function, blood dyscrasia), although combination opioids are *not recommended* for long-term use.

There is some evidence that dextromethorphan does not potentiate the effect of morphine opioids and therefore is *not recommended* to be used with opioids.

#### Evidence Statements Regarding Choice of Opioids, Indications, and Recommendations for Use

##### Strong Evidence

In patients being treated with opioid agonists for heroin addiction, methadone is more successful than buprenorphine at retaining patients in treatment. The rates of opiate use, as evidenced by positive urines, are equivalent between methadone and buprenorphine (Design: Meta-analysis of randomized trials).

Buprenorphine is superior to placebo with respect to retention in treatment (Design: Meta-analysis of randomized trials).

##### Good Evidence

Buprenorphine is superior to placebo with respect to positive urine testing for opiates (Design: Meta-analysis of randomized clinical trials).

In the setting of new onset chronic noncancer pain, there is a clinically important relationship between opioid prescription and subsequent opioid use disorder. Compared to no opioid use, short-term opioid use approximately triples the risk of opioid use disorder in the next 18 months. Use of opioids for over 90 days is associated with very pronounced increased risks of the subsequent development of an opioid use disorder, which may be as much as one hundredfold when doses greater than 120 MME are taken for more than 90 days. The absolute risk of these disorders is very uncertain but is likely to be greater than 6.1% for long duration treatment with a high opioid dose (Design: Retrospective cohort study using claims data from a large health care database).

Extended release tapentadol is more effective than placebo and comparable to oxycodone. The percent of patients who achieved 50% or greater pain relief was: placebo, 18.9%, tapentadol, 27.0%, and oxycodone, 23.3% (Design: Randomized clinical trial).

Transdermal buprenorphine is noninferior to oral tramadol in the treatment of moderate to severe musculoskeletal pain arising from conditions like osteoarthritis and low back pain. The population of patients for whom it is more appropriate than tramadol is not established but would need to be determined on an individual patient basis if there are clear reasons not to use oral tramadol (Design: Phase III noninferiority trial).

Transdermal fentanyl and transdermal buprenorphine are similar with respect to analgesia and sleep quality, and they are similar with respect to some common adverse effects such as constipation and discontinuation due to lack of effect. However, buprenorphine probably causes significantly less



nausea than fentanyl, and it probably carries a lower risk of treatment discontinuation due to adverse events. It is also likely that both transdermal medications cause less constipation than oral morphine (Design: Network meta-analysis of randomized clinical trials).

In the setting of common low back injuries, when baseline pain and injury severity are taken into account, a prescription for more than 7 days of opioids in the first 6 weeks is associated with an approximate doubling of disability one year after the injury (Design: Prospective cohort study).

#### Some Evidence

Long-acting oxycodone (Dazidox, Endocodone, ETH-oxydose, Oxycontin, Oxyfast, OxyIR, Percolone, Roxicodone) and oxymorphone have equal analgesic effects and side effects, although the milligram dose of oxymorphone (Opana) is half that of oxycodone (Design: Randomized clinical trial).

Extended release hydrocodone has a small and clinically unimportant advantage over placebo for relief of chronic low back pain among patients who are able to tolerate the drug and 40% of patients who begin taking the drug do not attain a dose which provides pain relief without unacceptable adverse effects. Hydrocodone extended release (ER) does not appear to improve function in comparison with placebo (Design: Randomized trial with a screening period of 7-14 days followed by an open-label titration period of up to 6 weeks followed by a double blind treatment period of up to 12 weeks).

In the setting of neuropathic pain, a combination of morphine plus nortriptyline produces better pain relief than either monotherapy alone, but morphine monotherapy is not superior to nortriptyline monotherapy, and it is possible that it is actually less effective than nortriptyline (Design: Crossover randomized trial).

Tapentadol can reduce pain to a moderate degree in diabetic neuropathy, average difference 1.4/10 pain scale, with tolerable adverse effects (Design: Randomized clinical trial).

Tapentadol causes less constipation than oxycodone (Design: Meta-analysis of randomized clinical trials).

Dextromethorphan does not potentiate the effect of morphine opioids and therefore is not recommended to be used with opioids (Design: Three randomized clinical trials).

Tramadol alleviates neuropathic pain following spinal cord injury (Design: Randomized clinical trial).

Tramadol yields a short-term analgesic response of little clinical importance relative to placebo in postherpetic neuralgia which has been symptomatic for approximately 6 months (Design: Randomized clinical trial).

#### Opioid Addiction Treatment

The methods of detoxification can include 1) abrupt discontinuation – *not recommended* due to high rate of relapse due to craving and withdrawal symptoms, 2) slow but progressive taper – 10% of total dosage per week as an outpatient treatment, 3) conversion to a different medication opioid (buprenorphine/naloxone) to enable a more stable and comfortable taper occasionally done as an outpatient but commonly done as part of a more comprehensive treatment program, and 4) rapid detox under anesthesia – *not recommended* due to relatively high incidence of complications and high expense.

See the original guideline document for definitions of opioid physical dependence, tolerance, opioid misuse, opioid abuse, pseudo-addiction, and addiction.

#### Evidence Statements Regarding Opioid Addiction Treatment

##### Strong Evidence

In patients being treated with opioid agonists for heroin addiction, methadone is more successful than buprenorphine at retaining patients in treatment. The rates of opiate use, as evidenced by positive urines, are equivalent between methadone and buprenorphine (Design: Meta-analysis of randomized clinical trials).

##### Opioid/Chemical Treatment Programs

Chemical dependency for workers' compensation issues will usually be related to opioids, anxiolytics, or

hypnotics as prescribed for the original workers' compensation injury. Chemical dependency should be treated with specific programs providing medical and psychological assessment, treatment planning, and individual as well as group counseling and education. Established functional goals which are measurable, achievable, and time specific are required.

See the original guideline document for time to produce effect, frequency, and optimum and maximum durations.

#### Orthotics/Prosthetics/Equipment

Devices and adaptive equipment are rarely necessary for CRPS patients as motion is to be encouraged. Specific devices may be useful in rare cases to aid in return-to-work duties.

#### Personality/Psychological/Psychosocial/Psychiatric Intervention

Psychosocial treatment is a well-established therapeutic and diagnostic intervention with selected use in acute pain problems and more widespread use in sub-acute and chronic pain populations. Psychosocial treatment is recommended as an important component in the total management of a patient with CRPS and should be implemented as soon as the problem is identified.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for indications, evidence, and time frames.

#### Restriction of Activities

Continuation of normal daily activities is the recommendation for most patients since immobility will negatively affect rehabilitation. Prolonged immobility results in a wide range of deleterious effects, such as a reduction in aerobic capacity and conditioning, loss of muscle strength and flexibility, increased segmental stiffness, promotion of bone demineralization, impaired disc nutrition, and the facilitation of the illness role.

Some level of immobility may occasionally be appropriate which could include splinting/casting or as part of a structured schedule that includes energy conservation or intentional rest breaks between activities. While these interventions may occasionally have been ordered in the acute phase, the provider should be aware of their impact on the patient's ability to adequately comply with and successfully complete rehabilitation. Activity should be increased based on the improvement of core strengthening.

Patients should be educated to the detrimental effects of immobility versus the efficacious use of limited rest periods. Adequate rest allows the patient to comply with active treatment and benefit from the rehabilitation program. In addition, complete work cessation should be avoided, if possible, since it often further aggravates the pain presentation and promotes disability. Modified return-to-work is almost always more efficacious and rarely contraindicated in the vast majority of injured workers with chronic pain.

#### Return-to-Work

Return-to-work and/or work-related activities whenever possible is one of the major components in treatment and rehabilitation. Return-to-work is a subject that should be addressed by each workers' compensation provider at the first meeting with the injured employee and updated at each additional visit. A return-to-work format should be part of a company's health plan, knowing that return to work can decrease anxiety, reduce the possibility of depression, and reconnect the worker with society.

A prolonged time off work is likely to lead to chronic disability. In complex cases, experienced nurse case managers may be required to assist in return to work. Other services, including psychological evaluation and/or treatment, jobsite analysis, and vocational assistance, may be employed.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for considerations and recommendations.

#### Therapy—Active

The following active therapies are widely used and accepted methods of care for a variety of work-related injuries. Active therapy is based on the philosophy that therapeutic exercise and/or activity can alleviate discomfort and are beneficial for restoring flexibility, strength, endurance, function, and range-of-motion. All active therapy plans should be made directly with patients in the interest of achieving long-term individualized goals.

### *Pain Neuroscience Education*

#### Evidence Statements Regarding Patient Education

##### Good Evidence

Pain neuroscience education combined with a physical intervention is more effective in reducing pain, improving disability, and reducing healthcare utilization compared with either usual care, exercise, other education or another control group for the treatment of patients with chronic musculoskeletal pain (Design: Narrative systematic review of randomized clinical trials).

##### Some Evidence

A cognitive intervention consisting of 2 consultations lasting 1 hour each with a physical medicine specialist and a physical therapist covering coping strategies and patient education on motion produces short-term reductions in sub-acute back disability (Design: Randomized clinical trial). In the setting of non-specific chronic low back pain, patient-centered cognitive functional therapy from physical therapists produced superior outcomes for pain reduction and functional improvement compared with traditional manual therapy and exercise at post-intervention and at 12-month follow-up (Design: Single-blind randomized clinical trial).

The following active therapies are listed in alphabetical order:

- Activities of daily living (ADL)
- Aquatic therapy
- Functional activities
- Gait training
- Mirror therapy—graded motor imagery
- Neuromuscular re-education
- Stress loading
- Therapeutic exercise
- Work conditioning
- Work simulation

### *Aquatic Therapy*

#### Evidence Statements Regarding Aquatic Therapy

##### Good Evidence

Aquatic exercise and land-based exercise show comparable outcomes for function and mobility among people with symptomatic osteoarthritis of the knee or hip (Design: Systematic review and meta-analysis of randomized clinical trials).

### *Mirror Therapy—Graded Motor Imagery*

#### Evidence Statements Regarding Mirror Therapy—Graded Motor Imagery

##### Some Evidence

Mirror box therapy 30 minutes per day for 4 weeks is likely to reduce pain in CRPS (Design: Randomized clinical trial, systematic review and meta-analysis).

### *Neuromuscular Re-education*

## Evidence Statements Regarding Neuromuscular Re-education

### Some Evidence

There is a modest benefit from adding a back school to other treatments such as NSAIDs, massage, transcutaneous electrical nerve stimulation (TENS), and other physical therapy modalities (Design: Systematic review of randomized clinical trials).

### *Therapeutic Exercise*

## Evidence Statements Regarding Therapeutic Exercise

### Strong Evidence

In the short, intermediate, and long-term, motor control exercises that emphasize the transversus abdominis and multifidi are at least as effective as other forms of exercise and manual therapy. They are possibly more effective than other minimal interventions in reducing pain and improving disability in patients for the treatment of chronic non-specific low back pain (Design: Meta-analyses of randomized clinical trials).

### Good Evidence

A 12 week course of treatment in the McKenzie method is at most modestly more effective than spinal manipulation of similar duration in reducing disability in patients with persistent (more than 6 weeks duration, mean = 95 weeks) nonspecific low back pain, although a clinically relevant difference was not apparent. The McKenzie method should not be utilized if there is severe nerve root involvement with motor, sensory, or reflex abnormality (Design: Randomized clinical trial). Pilates is more effective in reducing pain and improving disability compared with a minimal intervention at intermediate term follow-up, but Pilates is equally as effective as other forms of exercise in improving disability at short- or intermediate-term follow-up for the treatment of patients with chronic non-specific low back pain (Design: Meta-analyses of randomized clinical trials). Exercise alone or part of a multi-disciplinary program results in decreased disability for workers with non-acute low back pain (Design: Meta-analysis of randomized clinical trials).

### Some Evidence

An unsupervised 12-week, periodized musculoskeletal rehabilitation program of weight training conducted 2, 3, or 4 days a week is effective at improving musculoskeletal strength and quality of life and at reducing pain and disability in untrained persons with chronic low back pain. The 4 days a week training volume is most effective. The volume (total number of reps) of progressive muscle relaxation (PMR) exercise prescribed is important (Design: Randomized clinical trial). Trunk balance exercises combined with flexibility exercises are more effective than a combination of strength and flexibility exercises in reducing disability and improving physical function in patients with chronic low back pain (Design: Single-blind randomized clinical trial). An exercise program which includes resistance training of the cervical and scapulothoracic muscles, combined with stretching of the same muscles, is likely to be beneficial for mechanical neck pain. Cervicoscapular endurance exercises are beneficial for chronic cervicogenic headache. General fitness exercises and upper extremity exercises are unlikely by themselves to be beneficial for mechanical neck pain and are therefore *not recommended* (Design: Meta-analysis of randomized clinical trials). There is no significant difference in the effectiveness of a 12-week, 20 session comprehensive supervised exercise program and an unsupervised simple exercise program with advice for improvement in average pain intensity in the preceding week in people with a mild chronic whiplash-associated disorder even though both interventions resulted in small reductions of pain over 12 months (Design: Assessor single-blind randomized clinical trial). A 4-month intervention for chronic neck pain patients containing pain education, specific exercises and graded activity training shows a significant effect, although clinically small, on improved physical and mental health related quality of life compared with controls receiving pain education alone. Good adherence increased the effect in favor of the exercise group (Design: Assessor single-blind

randomized controlled superiority multicenter clinical trial).

12 weeks of supervised high-dose exercise, spinal manipulative therapy, or low-dose home exercise with advice are all equally effective for reducing pain in the short- and long-term (one year) in those who have chronic low back pain (Design: Assessor single-blinded randomized controlled trial).

Intensive exercise coupled with cognitive behavioral therapy is as effective for chronic un-operated low back pain as posterolateral fusion (Design: Randomized clinical trial).

In the setting of non-specific chronic low back pain, patient-centered cognitive functional therapy from physical therapists produced superior outcomes for pain reduction and functional improvement compared with traditional manual therapy and exercise at post-intervention and at 12-month follow-up (Design: Single-blind randomized clinical trial).

There is no significant difference in the effectiveness of an 8-week supervised walking program, an evidence-based group exercise class, and usual physiotherapy for improvement in functional disability after 6 months for people with chronic low back pain even though all 3 interventions resulted in small, significant improvements in physical function, reduction of pain, quality of life, and fear avoidance over time (Design: Assessor single-blind randomized clinical trial).

### Evidence Statements Regarding Yoga

#### Strong Evidence

Yoga has small to moderate advantages over providing only a booklet in reducing low back pain and back-specific disability, but there is no evidence that yoga is superior to stretching and strengthening classes led by a licensed physical therapist (Design: Meta-analysis of randomized clinical trials).

#### Good Evidence

In the setting of chronic low back pain, 8 weeks of 2 hour weekly group sessions of either mindfulness based stress reduction meditation program with yoga or cognitive behavioral therapy results in small, significant improvements in physical function and reduction in pain compared to usual care at 26 weeks with no significant differences in outcomes between the 2 treatments (Design: Single-blind randomized clinical trial).

#### Some Evidence

Iyengar yoga, which avoids back bending, results in improved function and decreased chronic mechanical low back pain for up to 6 months. Instruction occurred 2 times per week for 24 weeks and was coupled with home exercise. One quarter of the participants dropped out (Design: Randomized clinical trial).

In the setting of chronic pain, both an 8-week mindfulness based stress reduction meditation program with yoga and an 8-week multidisciplinary pain intervention program with exercise resulted in small, significant reductions in pain intensity and pain-related distress post intervention but with no significant differences in outcomes between the 2 programs (Design: Single-blind randomized clinical trial).

See the original guideline document for time to produce effect, frequency, training period, optimum and maximum durations, and indications.

#### Therapy—Passive

Refer to the original guideline document for a description of the following passive therapies including time to produce effect, frequency, and optimum and maximum duration of treatment:

Continuous passive motion (CPM)

Desensitization

Fluidotherapy

Paraffin bath

Superficial heat therapy

### Therapeutic Procedures—Operative

When considering operative intervention in CRPS management, the treating physician must carefully consider the inherent risk and benefit of the procedure. All operative intervention should be based on a positive correlation with clinical findings, the clinical course, and diagnostic tests. A comprehensive assessment of these factors should have led to a specific diagnosis of confirmed CRPS with positive identification of the pathologic condition. Operative treatment is indicated when the natural history of surgically treated lesions is better than the natural history for non-operatively treated lesions.

Surgical procedures are seldom meant to be curative and would be employed in conjunction with other treatment modalities for maximum functional benefit. Functional benefit should be objectively measured and includes the following:

- Return-to-work or maintaining work status
- Fewer restrictions at work or performing activities of daily living
- Decrease in usage of medications prescribed for the work-related injury
- Measurable functional gains, such as increased range of motion (ROM) or a documented increase in strength

Education of the patient should include the proposed goals of the surgery, expected gains, risks or complications, and alternative treatment.

Smoking may affect soft tissue healing through tissue hypoxia. Patients should be strongly encouraged to stop smoking and be provided with appropriate counseling by the physician. If a treating physician recommends a specific smoking cessation program peri-operatively, this should be covered by the insurer. Physicians may monitor smoking cessation with laboratory tests such as cotinine levels. The surgeon will make the final determination as to whether smoking cessation is required prior to surgery. Similarly, patients with uncontrolled diabetes are at increased risk of post-operative infection and poor wound healing. It is recommended that routine lab work prior to any surgical intervention include a hemoglobin A1c. If it is higher than the recommended range, the surgery should be postponed until optimization of blood sugars has been achieved.

Prior to surgical intervention, the patient and treating physician should identify functional operative goals and the likelihood of achieving improved ability to perform activities of daily living or work activities, and the patient should agree to comply with the pre- and post-operative treatment plan including home exercise. The provider should be especially careful to make sure the patient understands the amount of post-operative therapy required and the length of partial- and full-disability expected post-operatively.

#### Neurostimulation

Spinal cord stimulation (SCS) is the delivery of low-voltage electrical stimulation to the spinal cord or peripheral nerves to inhibit or block the sensation of pain. The system uses implanted electrical leads and a battery powered implanted pulse generator.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for indications and evidence.

#### Dorsal Root Ganglion Stimulator

##### Evidence Statements Regarding Dorsal Root Ganglion Stimulator

###### Good Evidence

Dorsal root ganglion stimulation is non-inferior to conventional spinal cord stimulation (SCS) with respect to pain relief for CRPS patients with lower extremity pain (Design: Randomized non-inferiority clinical trial).

###### Some Evidence

Dorsal root ganglion stimulation is superior to spinal cord stimulation with respect to pain relief for up to 12 months after implantation. Neurological deficits related to stimulation with either device appear to be

rare. 46% of the DRG patients had more serious complications compared to 26% for SCS (Design: Randomized non-inferiority clinical trial).

Refer to the original guideline document for complications, surgical indications, contraindications, operative treatment, post-operative considerations, and post-operative therapy

#### Peripheral Nerve Stimulation

There are no randomized controlled studies for this treatment. This modality should only be employed with a clear nerve injury or when the majority of pain is clearly in a nerve distribution in patients who have completed 6 months of other appropriate therapy including the same pre-trial psychosocial evaluation and treatment as are recommended for spinal cord stimulation. A screening trial should take place over 3 to 7 days and is considered successful if the patient meets both of the following criteria: (a) experiences a 50% decrease in pain, which may be confirmed by VAS or Numerical Rating Score (NRS) and (b) demonstrates objective functional gains or decreased utilization of pain medications. Objective, measurable, functional gains must be evaluated by an occupational therapist and/or physical therapist and the primary treating physician (who did not place the nerve stimulator) prior to and before discontinuation of the trial. It may be used for proven occipital, ulnar, median and other isolated nerve injuries.

#### Intrathecal Drug Delivery

*Not generally recommended.* Requires prior authorization. Due to conflicting studies in this population and complication rate for long-term use, it may be considered only in very rare occasions when dystonia and spasticity are dominant features or when pain is not able to be managed using any other non-operative treatment.

Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for indications.

#### Sympathectomy, Including Use of Phenol or Radiofrequency

This procedure is generally *not recommended* and requires prior authorization. It may be considered for patients who are unable to return to normal activities of daily living when using the other non-operative treatments (as listed in "Therapeutic Procedures—Non-operative" above) and who meet the strict indications.

Indications – Single extremity CRPS-I with a significant amount of sympathetically mediated ischemia and distal pain only. The procedure should not be done if the proximal extremity is involved. Local anesthetic stellate ganglion block or lumbar sympathetic block consistently gives 90% to 100% relief each time a technically good block is performed and results in a temperature difference between the affected and the unaffected extremity of at least 1 degree Celsius. The procedure may be considered for individuals who have limited duration of relief from blocks. Permanent neurological complications are common.

#### Amputation

Amputation is *not recommended* in CRPS except in cases of gangrene or frequent/recurrent limb infections with the risk of osteomyelitis or systemic sepsis.

#### Maintenance Management

Successful management of chronic pain conditions results in fewer relapses requiring intense medical care. Failure to address long-term management as part of the overall treatment program may lead to higher costs and greater dependence on the health care system. Management of CRPS continues after the patient has met the definition of maximum medical improvement (MMI). MMI is declared when a patient's condition has plateaued and the authorized treating physician believes no further medical intervention is likely to result in improved function. Patients with either clinical or confirmed CRPS may qualify for an impairment when functional deficits exist related to CRPS physiology which are distinct from any other related conditions. When the patient has reached MMI, a physician must describe in detail the

maintenance treatment.

Maintenance care in CRPS requires a close working relationship between the carrier, the providers, and the patient. Providers and patients have an obligation to design a cost-effective, medically appropriate program that is predictable and allows the carrier to set aside appropriate reserves. Carriers and adjusters have an obligation to assure that medical providers can design medically appropriate programs. Designating a primary physician for maintenance management is strongly recommended.

Maintenance care will be based on principles of patient self-management. When developing a maintenance plan of care, the patient, physician and insurer should attempt to meet the following goals:

Maximal independence will be achieved through the use of home exercise programs or exercise programs requiring special facilities (e.g., pool, health club) and educational programs.

Modalities will emphasize self-management and self-applied treatment.

Management of pain or injury exacerbations will emphasize initiation of active therapy techniques and may occasionally require anesthetic injection blocks.

Dependence on treatment provided by practitioners other than the authorized treating physician will be minimized.

Reassessment of the patient's function must occur regularly to maintain daily living activities and work function.

Patients will understand that failure to comply with the elements of the self-management program or therapeutic plan of care may affect consideration of other interventions.

## Functional Tests

It is recommended that valid functional tests are used with treatments to track efficacy. Refer to the Division's [Chronic Pain Disorder Medical Treatment Guideline](#)  for Specific Maintenance Interventions and Parameters, including home exercise programs and exercise equipment, exercise programs requiring special facilities, patient education management, psychological management, non-opioid medication management, therapy management, and purchase or rental of durable medical equipment.

## Vitamin C

### Evidence Statements Regarding Vitamin C

#### Some Evidence

Vitamin C 500 mg taken for 50 days after a wrist fracture may help to prevent CRPS (Design: Randomized clinical trial).

## Opioid Medication Management

In very selective cases, scheduled opioids may prove to be the most cost effective means of ensuring the highest function and quality of life; however, inappropriate selection of these patients may result in a high degree of iatrogenic illness including addiction and drug overdose. A patient should have met the criteria in the opioids section of this guideline before beginning maintenance opioids. Laboratory or other testing may be appropriate to monitor medication effects on organ function. The following management is suggested for maintenance opioids:

The medications should be clearly linked to improvement of function, not just pain control. All follow-up visits should document the patient's ability to perform routine functions satisfactorily. Examples include the abilities to perform: work tasks, drive safely, pay bills or perform basic math operations, remain alert and upright for 10 hours per day, or participate in normal family and social activities. If the patient is not maintaining reasonable levels of activity the patient should usually be tapered from the opioid and tried on a different long-acting opioid.

A lower risk opioid medication regimen is defined as less than 50 MME per day. This may minimally increase or decrease over time. Dosages will need to be adjusted based on side effects of the medication and objective function of the patient. A patient may frequently be maintained on non-



opioid medications to control side effects, treat mood disorders, or control neuropathic pain; however, only one long-acting opioid and one short-acting opioid for rescue use should be prescribed. Buccally absorbed opioids other than buprenorphine are not appropriate for these non-malignant pain patients. Transdermal opioid medications are *not recommended*, other than buprenorphine.

All patients on chronic opioid medication dosages need to sign an appropriate opioid contract with their physician for prescribing the opioids.

The patient must understand that continuation of the medication is contingent on their cooperation with the maintenance program. Use of non-prescribed drugs may result in tapering of the medication. The clinician should order random drug testing at least annually and when deemed appropriate to monitor medication compliance.

Patients on chronic opioid medication dosages must receive them through one prescribing physician.

Refer to the original guideline document for maintenance duration.

## Injection Therapy

### *Sympathetic Blocks*

These injections are considered appropriate if they increase function for a minimum of 4 to 8 weeks. Maintenance blocks are combined with and are enhanced by the appropriate neuro-pharmacological medication(s) and an active self-management exercise program. It is anticipated that the frequency of the maintenance blocks may increase in the cold winter months or with stress.

Refer to the original guideline document for maintenance duration.

## Definitions

### Grades of Recommendation

Some means the recommendation considered at least one adequate scientific study, which reported that a treatment was effective. The Division recognizes that further research is likely to have an impact on the intervention's effect.

Good means the recommendation considered the availability of multiple adequate scientific studies or at least one relevant high-quality scientific study, which reported that a treatment was effective. The Division recognizes that further research may have an impact on the intervention's effect.

Strong means the recommendation considered the availability of multiple relevant and high-quality scientific studies, which arrived at similar conclusions about the effectiveness of a treatment. The Division recognizes that further research is unlikely to have an important impact on the intervention's effect.

## Clinical Algorithm(s)

None provided

## Scope

### Disease/Condition(s)

Complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy

## Guideline Category

Counseling

Management

Rehabilitation

Treatment

## Clinical Specialty

Family Practice

Internal Medicine

Neurological Surgery

Neurology

Physical Medicine and Rehabilitation

Psychiatry

Psychology

Rheumatology

Surgery

## Intended Users

Advanced Practice Nurses

Chiropractors

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Occupational Therapists

Patients

Physical Therapists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Substance Use Disorders Treatment Providers

Utilization Management

## Guideline Objective(s)

To provide advisory and educational guidelines for the treatment of complex regional pain syndrome/reflex sympathetic dystrophy that are enforceable under the Colorado Workers' Compensation Rules of Procedure

## Target Population

Individuals qualifying under Colorado's Workers' Compensation Act as injured workers with complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy (RSD)

## Interventions and Practices Considered

### Non-operative Therapeutic Procedures\*

- Acupuncture
- Biofeedback
- Complementary medicine
- Treatment of sleep disturbances
- Education/informed/shared decision making
- Therapeutic injections
  - Sympathetic injections
  - Peripheral nerve blocks
  - Other intravenous medications and regional blocks
  - Continuous brachial plexus infusions (not recommended)
  - Epidural infusion (not recommended)
  - Ketamine
- Interdisciplinary rehabilitation programs (formal and informal)
- Medications and medical management
  - Complex regional pain syndrome (CRPS)-specific medications (ketamine hydrochloride injections and calcitonin not recommended)
  - Alpha-acting agents
  - Anticonvulsants
  - Antidepressants
  - Hypnotics and sedatives
  - Marijuana (not recommended per federal law)
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Opioids
  - Skeletal muscle relaxants
  - Topical drug delivery
  - Tramadol
- Opioid addiction treatment
- Opioid/chemical treatment programs
- Orthotics/prosthetics equipment
- Personality/psychological/psychosocial/psychiatric interventions
- Restriction of activities
- Return to work
- Active therapy
  - Patient education
  - Activities of daily living (ADL)
  - Aquatic therapy
  - Functional activities
  - Gait training
  - Mirror therapy-graded motor imagery

- Neuromuscular re-education
- Stress loading
- Therapeutic exercise
- Work conditioning
- Work simulation
- Passive therapy
  - Continuous passive motion (CPM)
  - Fluidotherapy
  - Paraffin bath
  - Desensitization
  - Superficial heat therapy

#### Operative Therapeutic Procedures\*

- Neurostimulation
- Dorsal root ganglion stimulator
- Peripheral nerve stimulation
- Intrathecal drug delivery
- Sympathectomy
- Amputation

#### Maintenance Management

- Functional testing
- Vitamin C
- Opioid medication management
- Injection therapy (sympathetic blocks)

\*Note: See the "Major Recommendations" field and the original guideline document. Not all of the listed interventions and practices are recommended routinely or generally.

## Major Outcomes Considered

- Functional improvement (time to return to work, ability to return to original job, etc.)
- Change in pain scores (visual analogue scale, Oswestry Disability Questionnaire score, etc.)
- Duration of therapeutic effect
- Time to recovery
- Relapse rate
- Side effects or complications

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

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

#### General Literature Search Strategy

Studies were identified through the electronic database of PubMed (with specified search topics), and

from articles identified by searches. For some articles, the literature citation database Web of Science was used when it was desirable to find literature that cited a particular article. Relevant evidence statements from Cochrane and British Medical Journal (BMJ) Clinical Evidence were reviewed. Selected guidelines/systematic reviews were also reviewed. The reference lists from other literature and tables of contents from related journals were scanned for relevant articles (i.e., a hand search of literature was completed). Suggestions from various volunteer advisory bodies to the Division of Workers' Compensation were solicited.

Literature reviewed was in English. Literature searches were limited according to study type and human adults. Only randomized controlled trials (RCT) or meta-analyses were used for evidence statements regarding treatment. RCTs that compared an intervention with not using that intervention (e.g., surgery and non-operative treatment) were designated as more relevant to workers' compensation guidelines than those RCTs which compared variations on technique or types of devices.

Beginning with the Traumatic Brain Injury Medical Treatment Guideline Revision of 2012, RCTs may not have been critiqued individually if they were included in a critiqued meta-analysis of high quality. Relevant RCTs published after a Cochrane meta-analysis were evaluated as to whether they would have likely met the Cochrane inclusion criteria. If so, the Cochrane software (RevMan) was used to update the pooled effect measure and compare it with the original Cochrane report. Diagnostic accuracy studies were critiqued for diagnostic testing evidence. Cohort, cross-sectional and case-control studies were critiqued for causation evidence statements. Literature which did not meet requirements for evidence statements could be referenced if it furnished useful background information or described interventions which are considered generally accepted by a consensus of health care providers. This information sometimes contributed to consensus decisions by the multi-disciplinary task force drafting the guidelines. Literature that was determined either be unrelated to the clinical issue, did not reflect interventions likely to occur in Colorado, or which had such poor quality on initial review that it could not qualify for evidence nor provide meaningful input was not critiqued. All articles sent by the public were formally reviewed.

#### Specific Search Strategy

All searches were done on PubMed and the Cochrane Library. The literature search included articles published from January 2011 through July 2016. Search terms were complex regional pain syndrome and reflex sympathetic dystrophy syndrome.

#### Study Selection

Inclusion criteria: Studies in English; human; adults; RCT, systematic reviews, or meta-analysis

Exclusion criteria: Article titles containing an obvious mismatch with search criteria and search terms were eliminated (e.g., pediatric population, wrong condition). Abstracts were reviewed to exclude articles based on the following criteria:

- Lack of relevancy to workers' compensation population

- Major obvious errors in study protocol (e.g., lack of control group even though study was listed as an RCT)

- Study was included in a meta-analysis reviewed by Division staff (e.g., Cochrane Collaboration, BMJ Clinical Evidence)

- Study was published outside of time frame

- Cadaverous studies

- Preliminary results

- Healthy volunteers

- Studies not applicable to treatment guidelines conditions (e.g., tumor studies were excluded)

- Studies too technical in nature to meet the objective of the guideline (e.g., study comparing types of screws used in surgery)

Other literature was included in addition to sources identified by searches in the electronic databases. Some references were carried over from earlier versions of the guidelines. Other articles were selected by

hand searches of published literature. Articles submitted by the public and from volunteer advisory bodies to the Colorado Division of Workers' Compensation were also reviewed. All reviewed articles were included in the full Bibliography (included in this submission), but not all references qualified to be cited in the guideline. In total, 443 references were included in the full bibliography.

Included studies were reviewed for quality and relevancy. Some articles were excluded based on a "second tier" of exclusion criteria:

- Sample size too small <20 per group
- Animal study
- No outcomes of interest
- Population too old/young (<18 or >70)
- Study protocol and not an RCT
- Pilot study
- Surgical technique
- Included in a meta-analysis, systematic review, or Cochrane Review includes only one relevant RCT (RCT critiqued instead)
- No RCTs included (for a systematic review)
- Lack of assessor blinding (mainly drug studies)
- Inclusion criteria:  $\geq 3$  months of pain
- Not actually an RCT (lack of randomization)
- Narrative review
- Editorial
- Uninformative
- Not relevant or of interest
- Follow-up too short (<12 weeks)
- Study is too old (2010 or older)
- Article unobtainable or not in English
- Superseded by a more recent review
- No primary outcome
- Critiqued in previous version of the guideline

## Number of Source Documents

Number of articles identified by database search: 147

Number of articles included for review after exclusion criteria were applied to database search results: 45

Number of articles used to support evidence statements: 67

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

Subjective Review

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

See the [Colorado Division of Workers' Compensation Web site](#) , "Complex Regional Pain Syndrome/Reflex Sympathetic Dystrophy," for rating schemes for various types of studies.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

## Description of the Methods Used to Analyze the Evidence

Studies remaining after application of the exclusion criteria qualified for critique using the Division's Literature Critique Criteria. Studies assessed as "adequate" or "high quality" were used for evidence statements. Three levels ("some," "good," and "strong") were then used to describe strength of evidence for recommendations based on the amount and quality of the supporting literature. For more information regarding literature assessment and resulting evidence statements, see Chronic Pain Disorder on the Division's Web site for (a) Literature Critique Criteria, which are under "Assessment Criteria for Critiques" on the Web site, (b) the Evidence Summary/Table, and (c) Critiques for individual articles (see the "Availability of Companion documents" field).

Some articles were excluded after a critique was started, and reasons for exclusion were provided in the critique. A shortened version of the critique was completed if reasons for exclusion were identified early in the critique process.

Articles that were given a complete critique were given an assessment of "inadequate," "adequate," or "high quality." It should be noted that one article may be graded at different levels for different interventions. Also, in multiple cases, literature from the Cochrane Collaboration was reviewed. When Division of Workers' Compensation staff completed additional statistical pooling using RevMan (Cochrane Collaboration of Systematic Reviews), this is noted in the "Assessment by DOWC Staff" column of the critique.

For those studies deemed inadequate, a brief rationale was provided. The articles that were graded as either adequate or high quality were used for evidence statements. Three levels ("some evidence," "good evidence," and "strong evidence") were then used to describe strength of evidence for recommendations based on the amount and quality of the supporting literature. These levels of evidence are defined in the General Guidelines Principles, which are located in each of the Division Medical Treatment Guidelines.

Because the Division synthesizes the medical evidence as much as possible, one assessment (or group of assessments) may potentially create more than one evidence statement. It is also possible that multiple assessments may be combined for a higher level of evidence (e.g., two "adequate" studies might strengthen the evidence supporting a recommendation from "some" to "good").

Note that other recommendations in the Medical Treatment Guideline are consensus statements. Consensus statements are used only when adequate evidence was not available in the published literature reviewed by the Division or when published evidence was conflicting. The multidisciplinary Task Force makes consensus recommendations based on general medical principles and apply the following values: functional benefit to the patient, acceptable risk and morbidity, length of disability and timeframe to recovery, and lastly, acceptable cost. Consensus statements are often designated in Medical Treatment Guideline as "generally well accepted," "generally accepted," "acceptable/accepted," or "well-established."

## Methods Used to Formulate the Recommendations

Expert Consensus

Other

## Description of Methods Used to Formulate the Recommendations

Studies assessed as "adequate" or "high quality" were used for evidence statements. Three levels ("some," "good," and "strong") were then used to describe strength of evidence for recommendations based on the amount and quality of the supporting literature.

Expert Consensus statements were used when adequate evidence was not available in published literature or when published evidence was conflicting. Literature not meeting requirements for evidence statements was referenced if it described interventions which are generally accepted by a consensus of health care providers. This information, when available, contributed to consensus decisions for recommendations by the multi-disciplinary task force drafting the guidelines.

These recommendations were determined by the judgment of experienced professionals based on general medical principles. When making these recommendations, the task force considered the following values: functional benefit to patient, acceptable risk and morbidity, and length of disability and timeframe to recovery. Acceptable cost is considered, all else being equal. Consensus recommendations are typically designated with the language "generally well-accepted," "generally accepted," "acceptable/accepted," or "well-established."

#### Medical Treatment Guidelines - Updating Process

The Division's Medical Treatment Guidelines updating process is completed in several stages. Initially, current medical literature related to the guideline is reviewed, critiqued, and graded by the Division. Next, appropriate medical evidence and consensus are incorporated concurrently into the Guideline, section by section by the Division and a multidisciplinary Task Force. During this stage, Task Force members are sometimes appointed for projects, working in sub-groups or individually, according to the task. Guideline updating processes and resources dedicated by the Division to support the Task Force include:

- Medical literature review and grading, completed by a professional Research Methodologist and Epidemiologist,
- Evidence and consensus parameters to assist in the revision and evaluation of treatment recommendations,
- A multi-disciplinary Advisory Panel and other advisory bodies to provide clinical feedback to the Task Force and the Division,
- Administrative support and coordination, allowing participants to focus on clinical issues, and
- Opportunities for members to provide feedback on ways to improve the update process.

#### Selection of Task Force Members

Health care disciplines required to participate in the Task Force process are identified. Individuals selected should be Level I or II Accredited Providers (if applicable), Board Certified in their area of specialty, in good standing within their medical specialty organization, and specialize in treatment of injured workers. Task force membership also includes non-physician members of the workers' compensation system, such as: therapists, psychologists, attorneys, and risk managers. Prior task force participation is not necessary.

#### Medical Literature Review

Articles are selected for review based on relevance and informativeness after viewing their titles and abstracts. Published journal articles are selected to be critiqued by the research methodologist and epidemiologist prior to distribution. Unpublished articles or office handouts submitted by Task Force members or the public are reviewed and critiqued by the medical director, research methodologist and epidemiologist, who then communicate directly with the submitting individual regarding quality and relevance. The submitting individual retains the prerogative of distributing the material to the Task Force. Other unspecified material and public commentary received or solicited by the Division is reviewed and critiqued, as appropriate, and distributed at the discretion of the medical director and medical policy staff. Many articles are included in the bibliography without critiques or assessment for evidence. These articles are considered to provide pertinent information whether or not they lend themselves to formal evaluation for levels of evidence.

## Rating Scheme for the Strength of the Recommendations



## Grades of Recommendation

Some means the recommendation considered at least one adequate scientific study, which reported that a treatment was effective. The Division recognizes that further research is likely to have an impact on the intervention's effect.

Good means the recommendation considered the availability of multiple adequate scientific studies or at least one relevant high-quality scientific study, which reported that a treatment was effective. The Division recognizes that further research may have an impact on the intervention's effect.

Strong means the recommendation considered the availability of multiple relevant and high-quality scientific studies, which arrived at similar conclusions about the effectiveness of a treatment. The Division recognizes that further research is unlikely to have an important impact on the intervention's effect.

## Cost Analysis

Published cost analyses were reviewed.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

### Advisory Panel

The next stage of the guideline update process includes an additional review, conducted by an Advisory Panel and other advisory bodies that may consist of past Task Force members and knowledgeable professionals representing medical specialty organizations, associations, and other stakeholder groups. Professionals who represent adjunct aspects of patient care, such as risk managers, case managers, and insurers, are also included in this stage. The purpose of this review is to provide additional sources of expertise in order to finalize draft guideline material developed by the Task Force.

### Solicitation of Public Commentary

An active, open process to solicit public commentary is in place in order to maximize community-based physician and other stakeholder input and support. Contact with Accredited Providers is done through direct mailings and at Accreditation seminars.

### Post Task Force Questionnaire

A survey is sent to all Task Force members once the updated draft guidelines are completed. The survey rates Task Force participants' satisfaction with the process and evaluates Division personnel and performance. Information may be used to improve future Task Force processes.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is provided for each evidence statement (see the "Major Recommendations" field).

Only graded and critiqued randomized controlled trials or meta-analyses were used for evidence statements.

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

Optimal medical and functional outcomes for injured workers with complex regional pain syndrome/reflex sympathetic dystrophy

Evidence of benefits of specific treatment interventions is reviewed in the relevant sections of the original guideline document and in the evidence summary companion document (see the "Availability of Companion Documents" field).

## Potential Harms

- Injuries, side effects, or infections from therapeutic injections
- Side effects and drug interactions from medications
- Complications from operative procedures
- Injury from device or component failure

Refer to specific sections of the "Major Recommendations" field and original guideline document for detailed descriptions of potential harms.

# Contraindications

## Contraindications

- Absolute contraindications of diagnostic injections include (a) bacterial infection - systemic or localized to region of injection, (b) bleeding diatheses, (c) hematological conditions, and (d) possible pregnancy. Relative contraindications of these injections may include (a) allergy to contrast or shellfish, (b) poorly controlled diabetes mellitus and/or hypertension.
- Absolute contraindications of therapeutic injections include (a) bacterial infection - systemic or localized to region of injection, (b) bleeding diatheses, (c) hematological conditions, and (d) possible pregnancy. Relative contraindications of these injections may include (a) allergy to contrast or shellfish, (b) poorly controlled diabetes mellitus and/or hypertension.
- Contraindications for ketamine hydrochloride: can cause significant elevations in blood pressure.
- Contraindications for tramadol: use cautiously in patients who have a history of seizures, who are taking medication that may lower the seizure threshold, or taking medications that impact serotonin reuptake and could increase the risk for serotonin syndrome, such as monoamine oxidase inhibitors (MAO) inhibitors, selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and alcohol. Use with caution in patients taking other potential QT prolonging agents. Not recommended in those with prior opioid addiction. Has been associated with deaths in those with an emotional disturbance or concurrent use of alcohol or other opioids. Significant renal and hepatic dysfunction requires dosage adjustment.
- Extreme caution should be used in prescribing controlled substances for workers with one or more "relative contraindications."
  - History of alcohol or other substance abuse or a history of chronic benzodiazepine use.
  - Sleep apnea: If patient has symptoms of sleep apnea, diagnostic tests should be pursued prior

to chronic opioid use.

- Off work for more than 6 months with minimal improvement in function from other active therapy.
- Severe personality disorder or other known severe psychiatric disease per psychiatrist or psychologist.
- Monitoring of behavior for signs of possible substance abuse indicating an increased risk for addiction and possible need for consultation with an addiction specialist.
- Contraindications for dorsal root ganglion (DRG) stimulator include:
  - Unsuccessful trial: inability to obtain objective, documented, functional improvement, or reduction of pain.
  - Those with cardiac pacemakers should be evaluated on an individual basis as some may qualify for surgery.
  - Patients who are unable to properly operate the system.
  - Patients who are anti-coagulated and cannot be without anticoagulation for a few days (e.g., patients with artificial heart valves).
  - Patients with frequent severe infections.
  - Patients for whom a future magnetic resonance imaging (MRI) is likely.

See specific sections of the original guideline document for additional contraindications.

## Qualifying Statements

### Qualifying Statements

- To properly utilize this document, the reader should not skip nor overlook any sections.
- This document has been prepared by the Colorado Department of Labor and Employment, Division of Workers' Compensation (Division) and should be interpreted within the context of guidelines for physicians/providers treating individuals qualifying under Colorado's Workers' Compensation Act as injured workers with complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy (RSD).
- Although the primary purpose of this document is advisory and educational, these guidelines are enforceable under the Workers' Compensation Rules of Procedure, 7 CCR 1101-3. The Division recognizes that acceptable medical practice may include deviations from these guidelines, as individual cases dictate. Therefore, these guidelines are not relevant as evidence of a provider's legal standard of professional care.
- The Division provides procedures to implement medical treatment guidelines and to foster communication to resolve disputes among the provider, payer and patient through the Workers' Compensation Rules of Procedure. In lieu of more costly litigation, parties may wish to seek administrative dispute resolution services through the Division or the office of administrative courts.

## Implementation of the Guideline

### Description of Implementation Strategy

The principles summarized below are key to the intended implementation of all Division of Workers' Compensation guidelines and critical to the reader's application of the guidelines in the original guideline document.

**Application of Guidelines.** The Division provides procedures to implement medical treatment guidelines and to foster communication to resolve disputes among the provider, payer and patient through the Workers' Compensation Rules of Procedure. In lieu of more costly litigation, parties may

wish to seek administrative dispute resolution services through the Division or the office of administrative courts.

**Education.** 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 injuries and disability. 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 patients, employers, insurance systems, policy makers and the community as a whole. An education-based paradigm should always start with inexpensive communication providing reassuring and evidence-based information to the patient. More in-depth patient education is currently a component of treatment regimens which employ functional, restorative, preventive, and rehabilitative programs. 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. Facilitation through language interpretation, when necessary, is a priority and part of the medical care treatment protocol.

**Informed Decision Making.** Providers should implement informed decision making as a crucial element of a successful treatment plan. Patients, with the assistance of their health care practitioner, should identify their personal and professional functional goals of treatment at the first visit. Progress towards the individual's identified functional goals should be addressed by all members of the health care team at subsequent visits and throughout the established treatment plan. Nurse case managers, physical therapists, and other members of the health care team play an integral role in informed decision making and achievement of functional goals. Patient education and informed decision making should facilitate self-management of symptoms and prevention of further injury.

**Treatment Parameter Duration.** Time frames for specific interventions commence once treatments have been initiated, not on the date of injury. Obviously, duration will be impacted by patient adherence, as well as availability of services. Clinical judgment may substantiate the need to accelerate or decelerate the time frames discussed in the original guideline document.

**Active Interventions.** Active interventions emphasizing patient responsibility, such as therapeutic exercise and/or functional treatment, are generally emphasized over passive modalities, especially as treatment progresses. Generally, passive interventions are viewed as a means to facilitate progress in an active rehabilitation program with concomitant attainment of objective functional gains.

**Active Therapeutic Exercise Program.** Goals should incorporate patient strength, endurance, flexibility, coordination, and education. This includes functional application in vocational or community settings.

**Positive Patient Response.** Positive results are defined primarily as functional gains that can be objectively measured. Objective functional gains include, but are not limited to: positional tolerances, range-of-motion, strength, endurance, activities of daily living, ability to function at work, cognition, psychological behavior, and efficiency/velocity measures that can be quantified. Subjective reports of pain and function should be considered and given relative weight when the pain has anatomic and physiologic correlation. Anatomic correlation must be based on objective findings. Patient completed functional questionnaires such as those recommended by the Division as part of Quality Performance and Outcomes Payments (QPOP, see Rule 18-8) and/or the Patient Specific Functional Scale can provide useful additional confirmation.

**Re-evaluation of Treatment No Less Than Every 3 to 4 Weeks.** If a given treatment or modality is not producing positive results within 3 to 4 weeks, or within the time to produce effect in the guidelines, the treatment should be either modified or discontinued. Before discontinuing the treatment, the provider should have a detailed discussion with the patient to determine the reason for failure to produce positive results. Reconsideration of diagnosis should also occur in the event of poor response to a seemingly rational intervention.

**Surgical Interventions.** Surgery should be contemplated within the context of expected functional outcome and not purely for the purpose of pain relief. The concept of "cure" with respect to surgical treatment by itself is generally a misnomer. All operative interventions must be based upon positive correlation of clinical findings, clinical course, and diagnostic tests. A comprehensive assimilation of these factors must lead to a specific diagnosis with positive identification of pathologic conditions.

6-Month Time Frame. The prognosis drops precipitously for returning an injured worker to work once he/she has been temporarily totally disabled for more than 6 months. The emphasis within these guidelines is to move patients along a continuum of care and return-to-work within a 6-month time frame, whenever possible. It is important to note that time frames may be less pertinent for injuries that do not involve work-time loss or are not occupationally related.

Return-to-Work. A return-to-work is therapeutic, assuming the work is not likely to aggravate the basic problem or increase long-term pain. The practitioner must provide specific written physical limitations and the patient should never be released to non-specific and vague descriptions such as "sedentary" or "light duty." The following physical limitations should be considered and modified as recommended: lifting, pushing, pulling, crouching, walking, using stairs, bending at the waist, awkward and/or sustained postures, tolerance for sitting or standing, hot and cold environments, data entry and other repetitive motion tasks, sustained grip, tool usage and vibration factors. Even if there is residual chronic pain, return-to-work is not necessarily contraindicated. The practitioner should understand all of the physical demands of the patient's job position before returning the patient to full duty and should request clarification of the patient's job duties. Clarification should be obtained from the employer or, if necessary, from including, but not limited to: an occupational health nurse, occupational therapist, vocational rehabilitation specialist, an industrial hygienist, or another professional.

Delayed Recovery. Strongly consider a psychological evaluation, if not previously provided, as well as initiating interdisciplinary rehabilitation treatment and vocational goal setting, for those patients who are failing to make expected progress 6 to 12 weeks after initiation of treatment of an injury. Therefore, all chronic pain patients should have a documented psychological evaluation and psychological treatment as appropriate to address issue of chronic pain. It is also appropriate to clinically reassess the patient, function goals, and differential diagnosis. The Division recognizes that 3% to 10% of all industrially injured patients will not recover within the timelines outlined in the original guideline document despite optimal care. Such individuals may require treatments beyond the timelines discussed within the original guideline document, but such treatment requires clear documentation by the authorized treating practitioner focusing on objective functional gains afforded by further treatment and impact upon prognosis.

Guideline Recommendations and Inclusion of Medical Evidence. All recommendations are based on available evidence and/or consensus judgment. When possible, guideline recommendations will note the level of evidence supporting the treatment recommendation. It is generally recognized that early reports of a positive treatment effect are frequently weakened or overturned by subsequent research. When interpreting medical evidence statements in the guideline, the following apply:

Consensus means the judgment of experienced professionals based on general medical principles. Consensus recommendations are designated in the guideline as "generally well accepted," "generally accepted," "acceptable/accepted," or "well-established."

"Some evidence" means the recommendation considered at least one adequate scientific study, which reported that a treatment was effective. The Division recognizes that further research is likely to have an impact on the intervention's effect.

"Good evidence" means the recommendation considered the availability of multiple adequate scientific studies or at least one relevant high-quality scientific study, which reported that a treatment was effective. The Division recognizes that further research may have an impact on the intervention's effect.

"Strong evidence" means the recommendation considered the availability of multiple relevant and high quality scientific studies, which arrived at similar conclusions about the effectiveness of a treatment. The Division recognizes that further research is unlikely to have an important impact on the intervention's effect.

All recommendations in the guideline are considered to represent reasonable care in appropriately selected cases, irrespective of the level of evidence or consensus attached to them. Those procedures considered inappropriate, unreasonable, or unnecessary are designated in the guideline as "not recommended."

Treatment of Preexisting Conditions. The conditions that preexisted the work injury/disease will need to be managed under two circumstances: (a) a preexisting condition exacerbated by a work

injury/disease should be treated until the patient has returned to their objectively verified prior level of functioning or maximum medical improvement (MMI); and (b) a preexisting condition not directly caused by a work injury/disease but which may prevent recovery from that injury should be treated until its objectively verified negative impact has been controlled. The focus of treatment should remain on the work injury/disease.

This guideline document should be interpreted within the parameters of these guideline principles that may lead to more optimal medical and functional outcomes for injured workers.

## Implementation Tools

Chart Documentation/Checklists/Forms

Foreign Language Translations

Resources

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

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

### IOM Care Need

Getting Better

Living with Illness

### IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

Colorado Division of Workers' Compensation. Complex regional pain syndrome/reflex sympathetic dystrophy medical treatment guideline. Denver (CO): Colorado Division of Workers' Compensation; 2017 Nov 30. 96 p.

### Adaptation

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

### Date Released

## Guideline Developer(s)

Colorado Division of Workers' Compensation - State/Local Government Agency [U.S.]

## Source(s) of Funding

Colorado Division of Workers' Compensation

## Guideline Committee

Not stated

## Composition of Group That Authored the Guideline

Division staff include a medical director (MD, MPH, FACOEM) and two research staff who review and critique all literature used for recommendations (a research methodologist, MD, MSPH; and an epidemiologist, MS). Several other staff members are involved, including a unit supervisor (DPT), coordinator (PhD, CCC-SLP), and editor.

The external task force used to write recommendations included the following representatives: chiropractor, claimant's attorney (x2, one as alternate), doctor of osteopathic medicine, neurologist, nurse case manager, occupational medicine physician, occupational therapist, pain management physician (x2, one as alternate), pharmacist, physical medicine and rehabilitation physician (x3, one as a spinal cord stimulator specialist), physical therapist, psychologist, psychiatrist, and risk manager.

There was also an external advisory panel used to review the proposed guideline. The members who responded included the following professionals: attorney (x3; claimant's and respondent's), chiropractor (x2), doctor of osteopathic medicine, internal medicine physician, medical directors and experts from other states (x3), neurologist (x1), nurse case manager (x4), occupational medicine physician (x2), occupational therapist (x2), pain management doctor (x2), pharmacist (x2), physical medicine and rehabilitation physician (x3, one as a spinal cord stimulator specialist), physical therapist (x4), psychologist (x2), psychiatrist and risk manager (x2).

## Financial Disclosures/Conflicts of Interest

Every task force and advisory panel member completes a written disclosures and conflict of interest form.

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Colorado Division of Workers' Compensation. Complex regional pain syndrome/reflex sympathetic dystrophy: medical treatment guidelines. Denver (CO): Colorado Division of Workers' Compensation; 2011 Dec 27. 107 p.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Available from the [Colorado Division of Workers' Compensation Web site](#) .

## Availability of Companion Documents

The following are available:

Complex regional pain syndrome/reflex sympathetic dystrophy medical treatment guidelines. Referenced version. Denver (CO): Colorado Division of Workers' Compensation; 2017 Nov 30. 121 p. Available from the [Colorado Division of Workers' Compensation Web site](#) .

Complex regional pain syndrome/reflex sympathetic dystrophy medical treatment guideline 2017 revision. Search strategy and study selection. Denver (CO): Colorado Division of Workers' Compensation; 2017. 3 p. Available from the [Colorado Division of Workers' Compensation Web site](#) .

Complex regional pain syndrome/reflex sympathetic dystrophy medical treatment guideline 2017. Evidence summary and table. Denver (CO): Colorado Division of Workers' Compensation; 2017. 27 p. Available from the [Colorado Division of Workers' Compensation Web site](#) .

General literature search strategy for medical treatment guidelines. Denver (CO): Colorado Division of Workers' Compensation. 1 p. Available from the [Colorado Division of Workers' Compensation Web site](#) .

Division of Workers' Compensation medical treatment guidelines—methodology. Denver (CO): Colorado Division of Workers' Compensation. 10 p. Available from the [Colorado Division of Workers' Compensation Web site](#) .

In addition, related critiques are available from the [Colorado Division of Workers' Compensation Web site](#) . Assessment criteria for critiques are also available from the [Colorado Division of Workers' Compensation Web site](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on November 27, 2012. The information was verified by the guideline developer on December 28, 2012. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines. This summary was updated by ECRI Institute April 27, 2018. The updated information was verified by the guideline developer on April 30, 2018.

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