



## Complete Summary

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### GUIDELINE TITLE

Complex regional pain syndrome: treatment guidelines (third edition).

### BIBLIOGRAPHIC SOURCE(S)

Reflex Sympathetic Dystrophy Syndrome Association (RSDSA). Complex regional pain syndrome: treatment guidelines. Milford (CT): Reflex Sympathetic Dystrophy Syndrome Association (RSDSA); 2006 Jun. 67 p. [51 references]

### GUIDELINE STATUS

This is the current release of the guideline

This guideline updates a previous version: Reflex Sympathetic Dystrophy Syndrome Association (RSDSA). Clinical practice guidelines (second edition) for the diagnosis, treatment, and management of reflex sympathetic dystrophy/complex regional pain syndrome (RSD/CRPS). Milford (CT): Reflex Sympathetic Dystrophy Syndrome Association (RSDSA); 2002 Feb. 46 p. [47 references]

## \*\* REGULATORY ALERT \*\*

### FDA WARNING/REGULATORY ALERT

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

- [December 12, 2007, Carbamazepine](#): The U.S. Food and Drug Administration (FDA) has provided recommendations for screening that should be performed on specific patient populations before starting treatment with carbamazepine.
- [May 2, 2007, Antidepressant drugs](#): Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

## COMPLETE SUMMARY CONTENT

\*\* REGULATORY ALERT \*\*

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## SCOPE

### **DISEASE/CONDITION(S)**

Complex regional pain syndrome (CRPS), also known as:

- Reflex sympathetic dystrophy syndrome
- Causalgia (minor or major)

### **GUIDELINE CATEGORY**

Diagnosis  
Management  
Treatment

### **CLINICAL SPECIALTY**

Anesthesiology  
Internal Medicine  
Neurological Surgery  
Neurology  
Physical Medicine and Rehabilitation

### **INTENDED USERS**

Advanced Practice Nurses  
Health Care Providers  
Health Plans  
Managed Care Organizations  
Occupational Therapists  
Patients  
Physical Therapists  
Physician Assistants  
Physicians  
Psychologists/Non-physician Behavioral Health Clinicians

### **GUIDELINE OBJECTIVE(S)**

To provide recommendations for the treatment of complex regional pain syndrome (CRPS)

### **TARGET POPULATION**

Individuals with signs or symptoms suggestive of complex regional pain syndrome (CRPS)

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Diagnosis**

International Association for the Study of Pain (IASP) diagnostic criteria for complex regional pain syndrome (CRPS), including clinical and research versions

### **Management/Treatment**

1. Interdisciplinary management including occupational therapy, physical therapy, recreational therapy, vocational rehabilitation, and other therapeutic interventions (hyperbaric oxygen therapy, acupuncture, and chiropractic manipulation)
2. Pharmacotherapy
  - Anti-inflammatory drugs/immunomodulators
  - Anticonvulsants/neuromodulators
  - Antidepressants/anxiolytics
  - Opioids
  - N-methyl-D-aspartate (NMDA) receptor antagonists
  - Anti-hypertensives and alpha-adrenergic antagonists
  - Calcitonin
  - Bisphosphonates
  - Additional systemic drug treatment options
  - Topical treatments
3. Psychological interventions
  - Patient and family education
  - Psychological evaluation
  - Psychological pain management intervention
4. Interventional therapies
  - Sympathetic nerve blocks
  - Intravenous (IV) regional anesthetic blocks (IVRA)
  - Intravenous infusions
  - Other (brachial plexus/spinal blocks-infusions) blocks
  - Neurolytic sympathetic blocks (radiofrequency/alcohol-phenol)
  - Neurostimulation

## **MAJOR OUTCOMES CONSIDERED**

- Physical functioning
- Pain
- Health-related quality of life
- Sensitivity and specificity of diagnostic tests

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Searches of Electronic Databases

**DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

Not stated

**NUMBER OF SOURCE DOCUMENTS**

Not stated

**METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Subjective Review

**RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

Not applicable

**METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses  
Systematic Review

**DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

**METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Not stated

**RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

Not applicable

**COST ANALYSIS**

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

**METHOD OF GUIDELINE VALIDATION**

External Peer Review  
Internal Peer Review

**DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

#### Diagnostic Considerations

#### Revised Complex Regional Pain Syndrome (CRPS) Criteria Proposed by the Budapest Consensus Group

##### General Features of the Syndrome:

CRPS describes an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor and/or trophic findings. The syndrome shows variable progression over time.

There are two versions of the proposed diagnostic criteria: a clinical version meant to maximize diagnostic sensitivity with adequate specificity, and a research version meant to more equally balance optimal sensitivity and specificity.

##### Clinical Diagnostic Criteria for CRPS

1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in *three of the four* following categories:
  - *Sensory*: Reports of hyperesthesia and/or allodynia
  - *Vasomotor*: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
  - *Sudomotor/Edema*: Reports of edema and/or sweating changes and/or sweating asymmetry
  - *Motor/Trophic*: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Must display at least one sign\* at time of evaluation in *two or more* of the following categories:
  - *Sensory*: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
  - *Vasomotor*: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry
  - *Sudomotor/Edema*: Evidence of edema and/or sweating changes and/or sweating asymmetry
  - *Motor/Trophic*: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms

\*A sign is counted only if it is observed at time of diagnosis.

##### Research Diagnostic Criteria for CRPS

1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in *each of the four* following categories:
  - *Sensory*: Reports of hyperesthesia and/or allodynia
  - *Vasomotor*: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
  - *Sudomotor/Edema*: Reports of edema and/or sweating changes and/or sweating asymmetry
  - *Motor/Trophic*: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).
3. Must display at least one sign\* at time of evaluation in *two or more* of the following categories:
  - *Sensory*: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement).
  - *Vasomotor*: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry.
  - *Sudomotor/Edema*: Evidence of edema and/or sweating changes and/or sweating asymmetry.
  - *Motor/Trophic*: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).
4. There is no other diagnosis that better explains the signs and symptoms.

\*A sign is counted only if observed at time of diagnosis.

### **Interdisciplinary Management**

Because the symptoms of CRPS patients encompass all the bio-psycho-social complexities of chronic pain, the best hope of helping our patients is the adoption of a systematic, stable, empathetic and, above all, interdisciplinary approach that addresses those symptoms. Drugs, psychotherapy, and interventions should be efficiently deployed for patients who either cannot begin or fail to progress using the interdisciplinary approach (outlined in sections three through five in the original guideline document). Many patients will require medication and psychotherapy from the beginning to be successful in the pivotal functional restoration algorithm (see "A Sample Stepwise, Functional Restoration Algorithm" below). Treatment guidelines that center on progressive functional restoration delivered by an interdisciplinary team are traditional, have substantial empiric and anecdotal support, and have been assessed and ultimately codified by three large, expert, consensus-building conferences. Although high level evidence supporting the rationale for interdisciplinary treatment of CRPS is fairly sparse (as it is for any treatment of CRPS), much stronger evidence exists for the efficacy of the interdisciplinary approach in other pain conditions, such as chronic low back pain. That functional restoration can and should be the central intervention and outcome standard in CRPS is a theory that must be tested. Until then, the interdisciplinary approach for treating patients with CRPS remains the most pragmatic, helpful, and cost-effective therapeutic approach available today.

### **A Sample, Stepwise, Functional Restoration Algorithm**

<b>Step 1</b>	Reactivation
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	Contrast Baths Desensitization Exposure Therapy
<b>Step 2</b>	Flexibility Edema Control Isometric Strengthening Correction of Postural Abnormalities Diagnosis and Treatment of Secondary Myofascial Pain
<b>Step 3</b>	Range of Motion (ROM) (gentle) Stress Loading Isotonic Strengthening General Aerobic Conditioning Postural Normalization & Balanced Use
<b>Step 4</b>	Ergonomics Movement Therapies Normalization of Use Vocational/Functional Rehabilitation

From the outset, in appropriate cases, the patient should have access to medications and/or psychotherapy and/or injections. If the patient cannot begin, or fails to progress, at any step or in any regard, the clinical team should consider starting (or adding) more or stronger medications (see Pharmacotherapy below) and/or more intensive psychotherapies (see Psychological Interventions below) and/or different interventions (see Interventional Therapies below).

### **Pharmacotherapy**

**Pharmacotherapy Guide. The Following Strategies Are Suggested for Patients Who Have Been Diagnosed with CRPS but Who Cannot Begin or Progress in the Functional Restoration Algorithm \*:**

<b>Reason for inability to begin or progress</b>	<b>Action</b>
Mild-to-moderate pain	Simple analgesics and/or blocks (see section 5 in the original guideline document)
Excruciating, intractable pain **	Opioids and/or blocks or later, more experimental interventions (see section 5 in the original guideline document)

<b>Reason for inability to begin or progress</b>	<b>Action</b>
Inflammation/swelling and edema	Steroids, systemic or targeted (acutely) or non-steroidal anti-inflammatory drugs (NSAIDs) (chronically); immunomodulators
Depression, anxiety, insomnia	Sedative, analgesic antidepressant/anxiolytics and/or psychotherapy (see section 3 in the original guideline document)
Significant allodynia/hyperalgesia	Anticonvulsants and/or other sodium channel blockers and/or N-methyl-D-aspartate (NMDA)-receptor antagonists
Significant osteopenia, immobility trophic changes	Calcitonin or bisphosphonates
Profound vasomotor disturbance	Calcium channel blockers, sympatholytics and/or blocks (section 5 in the original guideline document)

\*It is important to remember that these suggestions are overruled by individual patient presentation.

\*\*It is also important to note that certain drugs, such as bisphosphonates, may be associated with analgesia as well as the more primary action.

A methodical, patient approach to pharmacotherapy in CRPS is essential. To attempt to identify prominent mechanisms involved in the pain generation, and to try to match drug mechanisms of action to these is the *sine qua non* of the drug therapy of CRPS. It is often necessary to use more than one drug, or "rational polypharmacy," and the goal is often as much to relieve the pain as to allow progress in interdisciplinary rehabilitation. This is theoretically the best hope for comprehensive management of the syndrome, as drug therapy alone is never enough.

In most cases, no single drug will provide sufficient analgesia long term, nor will it completely prevent the need for abortive/rescue agents. This clinical reality usually requires two or even multiple medications to adequately manage the pain. Thus, the problem of drug-drug interaction is critical to consider, but unfortunately the literature is very weak in this regard. The traditional sources of information, such as the *Physician's Desk Reference*®, are somewhat helpful, but it is important to consider competitive metabolic or catabolic pathways, such as the liver cytochrome P450 catabolic systems. For instance, the 2D6 enzyme pathway catabolizes codeine, heterocyclic drugs, tramadol, mexiletine, and methadone (among others), and the prudent clinician would keep this in mind when combining these drugs. It is also important that if a drug-drug interaction is observed, this information should be reported and published.

Refer to the original guideline document for more information on individual drugs.

### **Psychological Interventions**

There is no solid evidence that psychological factors are necessarily involved in the onset of chronic CRPS. However, there are theoretically plausible pathways through which psychological factors in some cases *could* affect the development of CRPS. Evidence is mixed that CRPS patients are in any way psychologically unique

compared to other chronic pain patients, although the hypothesis that they are as a group more emotionally distressed has received some support. Once CRPS has developed, emotional factors may have a greater impact on CRPS pain intensity than in non-CRPS pain conditions, possibly through the impact of dysphoric psychological states on catecholamines. Meta-analytic reviews document the efficacy of various psychological interventions for many types of non-CRPS chronic pain, and suggest that such interventions are likely to be beneficial for CRPS patients as well. Adequate randomized controlled studies of psychological interventions in CRPS patients are not available to guide this aspect of CRPS management, although numerous uncontrolled studies suggest the likely utility of several approaches. These approaches include various forms of relaxation training, biofeedback, and cognitive and behaviorally focused interventions. Successful implementation of these interventions requires recognition of the unique issues in CRPS patients, particularly the pervasive learned (or centrally mediated) disuse often seen in such patients. Clinical experience using techniques like those described above in an integrated multidisciplinary context indicates that many CRPS patients can achieve significant improvements in functioning and ability to control pain.

**Psychological Intervention Treatment Algorithm**

<b>Step 1</b>	<p><b>Patient and Family Education about CRPS</b></p> <p>Pathophysiology (lay language)</p> <p>Disuse Issues</p> <p>Reactivation</p> <p>Self-Management Focus</p> <p>Possible Psychophysiological Interactions</p> <p>If patient has chronic CRPS or acute CRPS unresponsive to initial treatments</p>
<b>Step 2</b>	<p><b>Psychological Evaluation</b></p> <p>Comorbid Axis psychiatric disorders</p> <p>Cognitive, behavioral, emotional response to CRPS</p> <p>Ongoing life stressors</p> <p>Responses of significant others to CRPS</p>
<b>Step 3</b>	<p><b>Psychological Pain Management Intervention</b></p> <p>Relaxation training with feedback</p> <p>Cognitive intervention</p> <p>Reframing for active patient role</p>

	<p>Challenge dysfunctional cognitions</p> <p>Catastrophic cognitions</p> <p>Inaccurate beliefs about CRPS or treatment</p> <p>Cognitions underlying fear of movement</p> <p>Practice constructive self-talk</p> <p>Behavioral intervention</p> <p>Realistic pain-limited incremental reactivation</p> <p>Family intervention</p> <p>Address barriers to reactivation</p> <p>Increase constructive social support</p>
<b>Step 4</b>	If Axis I disorders or major life stressors are identified, conduct focused cognitive behavioral therapy targeting these issues

### **Interventional Therapies**

With a new understanding of CRPS as encompassing *both* sympathetically independent pain (SIP) and sympathetically maintained pain (SMP) in varying degrees among different patients, sympatholysis remains an important diagnostic (SMP vs. SIP) and therapeutic modality (in the SMP subgroup). Because of the considerable difficulty in "clinically assessing" the successful sympathetic block, and because "clinically successful" blocks provide varying degrees of sympatholysis, the role of local anesthetic injection sympathetic blockade versus intravenous regional anesthesia (IVRA), intravenous (IV), or epidural sympatholysis is unknown and largely based on local practice patterns. Additionally, with the notable paucity of good quality supportive outcomes studies, the clinician is left to utilize these blocks or sympathectomy-inducing infusions within the context of a broad algorithm of interdisciplinary treatment, while awaiting further pathophysiological data and outcomes research to guide our practice to the most beneficial treatments.

The decision to proceed with radiofrequency (RF) ablative techniques versus other nondestructive alternatives is a complex one, with less evidence for the ablative versus augmentative treatments. Due to the adverse long-term post sympathectomy syndromes, this author currently recommends against surgical ablative sympathectomy. Future studies may expand on the role of pulsed RF (cold RF) techniques or such unstudied techniques as cryosurgery as alternative therapies to treat SMP.

Our recommended strategy (and tactic) is to use interventional treatments for CRPS patients who are having difficulty either starting or progressing in the functional restoration/interdisciplinary algorithm. If patients are not progressing because of high pain levels (especially associated with autonomic dysfunction), then a stepwise progression — from the less invasive blocks, to infusions or

catheter infusion therapies, and ultimately perhaps to neurostimulation — is recommended in order to facilitate the patient's functional improvement and pain control. One suggested algorithm developed by an expert panel for the integrated use of these procedures is shown below and has been previously published.

**Interventional Pain Treatment Algorithm for CRPS\***

<b>Step 1</b>	<b>Minimally Invasive Therapies</b>  Sympathetic Nerve Blocks  Intravenous Regional Nerve Blocks  Somatic Nerve Blocks
<b>Step 2</b>	<b>More Invasive Therapies</b>  Epidural and Plexus Catheter Block(s)  Neurostimulation  Intrathecal Drug Infusion (e.g., Baclofen)
<b>Step 3</b>	<b>Surgical and Experimental Therapies</b>  Sympathectomy  Motor Cortex Stimulation

Inadequate or partial response to any given therapy should lead to a stepwise progression down through these modalities (moving from less to more invasive) in conjunction with other noninterventional treatments.

\*Adapted from Stanton-Hicks M, Burton A, Bruehl S, et al. An updated interdisciplinary clinical pathway for CRPS: report of an expert panel. Pain Practice. 2002;2:1-16.

**CLINICAL ALGORITHM(S)**

An additional clinical algorithm titled "Overall Treatment Algorithm (see other algorithms presented in the "Major Recommendations" field) is provided in the original guideline document.

**EVIDENCE SUPPORTING THE RECOMMENDATIONS**

**TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is not specifically stated for each recommendation.

**BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

**POTENTIAL BENEFITS**

- Appropriate, timely diagnosis and treatment of complex regional pain syndrome (CRPS)
- Restoration of function
- Minimization of pain
- Improved quality of life

## **POTENTIAL HARMS**

Complications of pharmacotherapy and interventional therapies

## **CONTRAINDICATIONS**

### **CONTRAINDICATIONS**

There are numerous, obvious contraindications to chronic steroid use.

## **IMPLEMENTATION OF THE GUIDELINE**

### **DESCRIPTION OF IMPLEMENTATION STRATEGY**

An implementation strategy was not provided.

### **IMPLEMENTATION TOOLS**

Clinical Algorithm  
Patient Resources  
Pocket Guide/Reference Cards  
Resources  
Slide Presentation

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**

Living with Illness

### **IOM DOMAIN**

Effectiveness  
Patient-centeredness

## **IDENTIFYING INFORMATION AND AVAILABILITY**

### **BIBLIOGRAPHIC SOURCE(S)**

Reflex Sympathetic Dystrophy Syndrome Association (RSDSA). Complex regional pain syndrome: treatment guidelines. Milford (CT): Reflex Sympathetic Dystrophy Syndrome Association (RSDSA); 2006 Jun. 67 p. [51 references]

## **ADAPTATION**

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

## **DATE RELEASED**

2002 Feb (revised 2006 Jun)

## **GUIDELINE DEVELOPER(S)**

Reflex Sympathetic Dystrophy Syndrome Association - Private Nonprofit Organization

## **SOURCE(S) OF FUNDING**

Funding has been provided by grants from the National Organization of Rare Disorders, Purdue Pharma L.P., and Celegene Corporation; donations from Reflex Sympathetic Dystrophy Syndrome Association (RSDSA) members; and from memorial gifts.

## **GUIDELINE COMMITTEE**

Scientific Advisory Committee

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Editor:* R. Norman Harden, MD

*Contributing Authors:* R. Norman Harden, MD; Stephen Bruehl, PhD; Allen Burton, MD; Melanie Swan, OTR/L; Brienne R. Costa, CTRS; Jennifer Barthel, MS; CRC; Amie L. King, PT

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Not stated

## **GUIDELINE STATUS**

This is the current release of the guideline

This guideline updates a previous version: Reflex Sympathetic Dystrophy Syndrome Association (RSDSA). Clinical practice guidelines (second edition) for the diagnosis, treatment, and management of reflex sympathetic dystrophy/complex regional pain syndrome (RSD/CRPS). Milford (CT): Reflex Sympathetic Dystrophy Syndrome Association (RSDSA); 2002 Feb. 46 p. [47 references]

## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [Reflex Sympathetic Dystrophy Syndrome Association \(RSDSA\) Web site](#).

Print copies: Available from the Reflex Sympathetic Dystrophy Syndrome Association; PO Box 502, Milford, CT 06460; Phone: 203-877-3790; Web site: [www.rsd.org](http://www.rsd.org)

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- Reflex sympathetic dystrophy (RSD)/complex regional pain syndrome (CRPS) slide kit. Reflex Sympathetic Dystrophy Syndrome Association (RSDSA); 2006 Oct. 36 p. Available from the [RSDSA Web site](#).
- TellTale signs of RSD/CRPS. Reflex Sympathetic Dystrophy Syndrome Association (RSDSA); 2006 2 p. Available from the [RSDSA Web site](#).

## **PATIENT RESOURCES**

Brochures and resource guides on concerns related to complex regional pain syndrome (CRPS) (e.g., sports injuries, helping children with CRPS succeed in school, hospital protocols, treatment and therapy options, government assistance programs, finding a specialist) are available from the [RSDSA Web site](#).

## **NGC STATUS**

This NGC summary was completed by ECRI on December 11, 2002. The information was verified by the guideline developer on January 27, 2003. This summary was updated by ECRI on January 12, 2005 following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of some non-steroidal anti-inflammatory drug products. This summary was updated on April 15, 2005 following the release of heightened warnings for nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on November 28, 2006. The updated information was verified by the guideline developer on November 30, 2006. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on January 10, 2008, following the U.S. Food and Drug Administration advisory on Carbamazepine.

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Date Modified: 11/3/2008

