

Notice of Independent Review Decision

**DATE OF REVIEW:** 10/04/2010

**IRO CASE #:**

**DESCRIPTION OF THE SERVICE OR SERVICES IN DISPUTE**

Medical necessity of medications refills previously non-certified on appeal: Norco, Ambien, Lyrica, Prozac, Mobic.

**A DESCRIPTION OF THE QUALIFICATIONS FOR EACH PHYSICIAN OR OTHER HEALTH CARE PROVIDER WHO REVIEWED THE DECISION**

The physician performing this review is Board Certified, American Board of Family Practice, Association of Certified Fraud Examiners, and American Board of Quality Assurance & Utilization Review Physicians. He is a member of National Medical Association, Association of Certified Fraud Examiners, American Health Lawyers Association, and Fellow of the American Institute for Health care Quality. He has been in practice since 1988.

**REVIEW OUTCOME**

Upon independent review the reviewer finds that the previous adverse determination/adverse determinations should be:

- Upheld (Agree)  
 Overturned (Disagree)  
 Partially Overturned (Agree in part/Disagree in part)

Provide a description of the review outcome that clearly states whether or not medical necessity exists for each of the health care services in dispute.

The applicable evidence based guidelines do not support prescription of Ambien for the treatment of claimant's current condition, based on the available documentation.

Applicable evidence based guidelines do not support prescription of Mobic for the treatment of claimant's current condition, based on the available documentation.

Applicable evidence based guidelines do not support prescription of Prozac as first line treatment for claimant's pain, based on the available documentation.

Applicable evidence based guidelines do not support prescription of Lyrica for the treatment of claimant's current condition, based on the available documentation.

Applicable evidence based guidelines do not support prescription of Norco for the treatment of claimant's current condition, based on the available documentation.

### **INFORMATION PROVIDED TO THE IRO FOR REVIEW**

Records Received: 24 page fax 9/17/2010 Texas Department of Insurance IRO request, 34 page fax 9/22/2010 from physician with office visit documentation, 12 scanned documents totaling 1,471 pages on 9/23/2010. Including 820 pages of clinical documentation, and additional review of three chapters of the ODG-TWC Integrated Treatment/Disability Duration Guidelines references (Shoulder, Neck and Upper Back, and Chronic Pain).

### **PATIENT CLINICAL HISTORY [SUMMARY]:**

The claimant is a man who was involved in a work injury on Xx/xx/xx. Records indicate that he was attempting to when he slipped on cement mud causing him to fall against it with his legs spread apart, as he tried to brace and catch himself with his outstretched right hand.

#### 2005 Notes:

The claimant was diagnosed with cervical radiculopathy and right shoulder pain with impingement as a result of the work incident. Initial reports also noted strain/sprain injury to the lumbar region, and pain in the groin where he reported to have been stuck by the hose as he slipped. Electrodiagnostic study reported C5-6 radiculopathy. MRI of the cervical spine noted degenerative disc disease, disc osteophyte complex, and foraminal narrowing C5-6. MRI of the right shoulder was reported to be normal. He was managed with physical therapy. Medication prescriptions included Hydrocodone/APAP on 6/17/05 and Mobic on 9/14/05. He received trigger point injections in his shoulder (Dr.). He received cervical ESI (MD) on 10/4/05, 11/1/05, 12/20/05 with partial pain relief reported. He also received subacromial bursal injection of the R shoulder ( MD) with reported 100% relief initially.

#### 2006 Notes

Chronic pain was documented to be ongoing in the right shoulder and neck with radiation into the shoulders, worse on the right than left. Additional Cervical ESI were performed

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on 3/1/06, 12/13/06. Cervical myelogram report noted C5-6 disc herniation with underfilling of nerve roots bilaterally and foraminal narrowing worse on the left. Consultation was completed with MD, who recommended anterior cervical discectomy and fusion surgery. Ambien was prescribed on 5/5/06 for reported sleep disturbance.

## 2007 Notes:

Operative Report (MD) dated 4/12/07 noted: anterior cervical discectomy with decompression and bilateral foraminotomies at C5-C6; anterior cervical fusion with placement of interbody fusion cage and cervical plate.

Postoperative visits stated that the claimant experienced some relief of neck pain and radiculopathy symptoms, however shoulder symptoms persisted. Repeat subacromial injection was administered to the right shoulder pain on 9/4/07, however shoulder pain persisted. Repeat shoulder MRI 12/18/07 was remarkable for partial tear of supraspinatus, and mild subacromial-subdeltoid bursitis, possible bucket handle SLAP tear, mild degenerative changes of AC joint.

## 2008 Notes:

Operative report dated 2/28/08 noted completion of right shoulder arthroscopic surgery with distal clavicle excision and biceps tenotomy for diagnoses of impingement syndrome, AC joint arthritis and Type 4 SLAP lesion with bicep tendonitis. Shoulder MRI was repeated on 5/7/08 for evaluation of persistent postoperative pain and limited shoulder ROM, noting a 3 mm loose body in the subcoracoid recess. Progress Notes documented persistent neck pain as well, reportedly decreased only 10% after the cervical fusion. Repeat cervical MRI with contrast was completed on 9/17/08, noting anterior cervical fusion with well positioned and anatomically aligned ventral hardware, and no postoperative abnormality or disc herniation. Electrodiagnostic studies completed on 11/6/08 (MD) noted no evidence of cervical radiculopathy, brachial plexopathy, or upper extremity neuropathy. Cervical ESI was performed on 12/8/08 (, MD)

## 2009 Notes:

Functional Capacity Evaluation completed on 1/13/09 noted limited active range of motion of the neck and right shoulder, with function at a sedentary to light physical demand level. Another cervical ESI was performed on 1/16/09 (Dr.). Progress Notes on 1/20/09 by both MD & Dr. reported some improvement in neck pain following cervical ESI and also improvement in shoulder pain after the arthroscopic surgery and subacromial injections.

2/11/09 – 4/17/09 notes report consultation and treatment with CoPE program for multidisciplinary chronic pain management documented ongoing problems with insomnia and depression. It was noted that the claimant had been unemployed since August 2005. Treatment at CoPE included prescriptions for Prozac and Trazadone, with reported improvement in strength, ROM, activity tolerance, pain level, insomnia, anxiety, and depression. Neck pain was reported to be significantly improved, with only limited relief of shoulder pain.

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4/23/09 Progress Note (Dr. suggests that the claimant might have reinjured his shoulder while lifting household items during a move. Dr. suggested that difficulty to substantially reduce pain medications was due to shoulder pain. Dr. stated that the claimant told him that Lyrica was not helpful.

Independent Medical Exam performed on 6/3/09 (, MD) recommended discontinuation (tapering and weaning where necessary) of medications which were not deemed to have been efficacious and/or exceeded guidelines recommendations, including Zanaflex, Ambien, Ibuprofen, Trazadone, Prozac, and Lyrica. Dr. suggested potential benefit from substituting medications such as Elavil antidepressant and Tramadol for pain.

2010 Notes:

1/21/10 Progress Note (MD) dictated by PA-C) stated that an attempted medication taper was not working very well. Further details of the taper were not included. He was reported to still have significant pain and insomnia despite trial of Amitriptyline and Unisom Recommendation was for pain management referral. Lyrica, and Mobic were to be continued for another two months, and he was given prescriptions for two months of Norco q.i.d. and Ambien 5 mg hs.

1/28/10 Progress Note (Dr.) stated that Amitriptyline and Ultram were not helpful, and were therefore discontinued. Norco was tapered to 4 tabs daily, but was unable to taper to 3 tabs daily. Depressive symptoms reportedly recurred after he ran out of Prozac.

3/3/10 Progress Note (Dr.) stated that he had gotten refills of his medicines and was “doing better in that regard on all fronts.” No objective or functional data was documented.

4/22/10 Peer Review (, MD) recommended reassessment of pain management, and reiterated his recommendation for Elavil and Ultram, with discontinuation of other medications including weaning off of Norco.

7/13/10 Progress Note (Dr. stated he was having trouble getting his meds after a peer review was completed. The claimant reported being unable to drive to visit his daughter in Abilene, and just has to lie around when he is off of his medications. He reported ability to mow the yard, water plants, garden, and putter around the house while taking medications. He reportedly was continuing to take Prozac 20 mg, Mobic 15 mg, Lyrica 75 mg bid, Ambien 5 mg hs, Norco 10 mg qid, “trying to stretch out his meds.” Exam noted tenderness in the right greater than rhomboids and posterior shoulder, positive Lhermitte’s and positive Spurling maneuver on the right, decreased right shoulder range of motion especially with abduction and external rotation, decreased right triceps reflex, and normal sensory exam. Dr. diagnoses were cervical syndrome with possible radiculitis. “Plan” was to obtain authorization for medications refills, and return visit in 6 months. Prescriptions were written for the following:

Norco 10 mg-325 mg Tab: Take 1 tablet(s) by oral route QID PRN. Qty: 120 Refills: 5

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Ambien 5 mg Tab: Take 1 tablet by oral route once daily at bedtime as needed. Qty: 30 Refills 5

Prozac 20 mg Cap: Take 1 Capsule by oral route daily. Qty: 30 Refills: 5

Lyrica 75 mg Cap: Take 1 Capsule by oral route BID. Qty: 60 Refills: 5

Mobic 15 mg Tab: Take 1 tablet by oral route once daily. Qty: 30 Refills: 5

## **ANALYSIS AND EXPLANATION OF THE DECISION INCLUDE CLINICAL BASIS, FINDINGS AND CONCLUSIONS USED TO SUPPORT THE DECISION.**

### **Ambien (Zolpidem) 5 mg, 1 tab at bedtime as needed #30 [5 refills]:**

The applicable evidence based guidelines do not support prescription of Ambien for the treatment of claimant's current condition, based on the available documentation.

The applicable ODG Guidelines support short-term Ambien prescription (two – to six weeks), which has been exceeded in this case. ODG also mentions specific risks associated with continued Ambien use, including increased pain and depression with long-term use, impaired function and memory, and habit formation.

### **Mobic (Meloxicam) 15 mg, 1 tab daily #30 [5 refills]:**

Applicable evidence based guidelines do not support prescription of Mobic for the treatment of claimant's current condition, based on the available documentation.

Treatment Guidelines state that there is no proven benefit of prescription NSAID such as Mobic over 1<sup>st</sup> line recommended Acetaminophen. Guidelines additionally caution that concurrent use of SSRIs and NSAIDs is associated with moderate excess relative risk of serious upper GI events, and that the risk is greatest with selected SSRIs (including Prozac) that have the highest degree of inhibition of serotonin reuptake.

### **Prozac (Fluoxetine) 20 mg, 1 capsule daily #30 [5 refills]:**

Applicable evidence based guidelines do not support prescription of Prozac as first line treatment for claimant's pain, based on the available documentation.

An alternate class of anti-depressants (tricyclics) is recommended as first line treatment for chronic neuropathic pain, and as an option for non-neuropathic pain that is refractory to analgesics and anti-inflammatory medications. Additionally, there is an increased risk of serious upper GI side effects when Prozac is used in combination with NSAIDS.

### **Norco (Hydrocodone / Acetaminophen) 10/325, 1 tab four times daily as needed #120 [5 refills]:**

Applicable evidence based guidelines do not support prescription of Norco for the treatment of claimant's current condition, based on the available documentation.

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Treatment guidelines support short-term use of opioids. However, long-term efficacy is not established. Guidelines mention risks of tolerance and addiction, and state that pain may be improved with weaning of opioids. Guidelines also recommend monitoring of outcomes including functional capacity improvement to guide treatment, rather than simply focusing on pain severity. Documentation in this case is insufficient in detailing outcomes and objective measures of functional status.

**Lyrica (Pregabalin) 75 mg, 1 capsule twice daily #60 [5 refills]:**

Applicable evidence based guidelines do not support prescription of Lyrica for the treatment of claimant's current condition, based on the available documentation.

Lyrica is FDA approved for use in diabetic neuropathy and post herpetic neuralgia. While it is sometimes used in 'off label' fashion for other conditions causing neuropathic pain, careful monitoring of outcomes and functional improvement is necessary to substantiate medical necessity. Documentation of outcomes and objective measures of function in this case does not sufficiently detail to provide evidence of efficacy from treatment with Lyrica. Documentation does not sufficiently detail trials and outcomes of treatment with the recommended first line medications for chronic pain treatment. Additionally, a Progress Note dated 4/23/09 (Dr.) documents that the claimant stated that Lyrica was not helpful.

**A DESCRIPTION AND THE SOURCE OF THE SCREENING CRITERIA OR OTHER CLINICAL BASIS USED TO MAKE THE DECISION:**

- ACOEM- AMERICAN COLLEGE OF OCCUPATIONAL & ENVIRONMENTAL MEDICINE UM KNOWLEDGEBASE
- AHCPR- AGENCY FOR HEALTHCARE RESEARCH & QUALITY GUIDELINES
- DWC- DIVISION OF WORKERS COMPENSATION POLICIES OR GUIDELINES
- EUROPEAN GUIDELINES FOR MANAGEMENT OF CHRONIC LOW BACK PAIN
- INTERQUAL CRITERIA
- MEDICAL JUDGEMENT, CLINICAL EXPERIENCE AND EXPERTISE IN ACCORDANCE WITH ACCEPTED MEDICAL STANDARDS
- MERCY CENTER CONSENSUS CONFERENCE GUIDELINES
- MILLIMAN CARE GUIDELINES
- ODG- OFFICIAL DISABILITY GUIDELINES & TREATMENT GUIDELINES (SEE BELOW)
- PRESSLEY REED, THE MEDICAL DISABILITY ADVISOR
- TEXAS GUIDELINES FOR CHIROPRACTIC QUALITY ASSURANCE & PRACTICE PARAMETERS
- TEXAS TACADA GUIDELINES
- TMF SCREENING CRITERIA MANUAL
- PEER REVIEWED NATIONALLY ACCEPTED MEDICAL LITERATURE (PROVIDE A DESCRIPTION)
- OTHER EVIDENCE BASED, SCIENTIFICALLY VALID, OUTCOME FOCUSED GUIDELINES (PROVIDE A DESCRIPTION)

## References:

From ODG Treatment Integrated Treatment/Disability Duration Guidelines **Shoulder** (Acute & Chronic) (updated 7-28-10):

Medications: For detailed information see the [Pain Chapter](#) of ODG Treatment.

From ODG Treatment Integrated Treatment/Disability Duration Guidelines **Neck & Upper Back** (Acute & Chronic) (updated 8-5-10):

For detailed information see the [Pain Chapter](#) of *ODG Treatment*. In this Neck Chapter, these listings may also be relevant: [Botulinum toxin](#) (injection); [Chymopapain](#) (injection); [Corticosteroid injection](#); [Epidural steroid injection \(ESI\)](#); [Facet joint therapeutic steroid injections](#); [Greater occipital nerve block, therapeutic](#); [High-dose methylprednisolone](#); [Iliac crest donor-site pain treatment](#); [Injections](#); [Methylprednisolone](#); [Muscle relaxants](#); [Nonprescription medications](#); [Occipital nerve block](#); [Opioids](#); [Oral corticosteroids](#); [Postoperative pain pump](#); [Steroids](#).

**Opioids:** Not recommended except for short use of opioids for severe cases, not to exceed 2 weeks. See also the [Pain Chapter](#). When used only for a time-limited course, opioid analgesics are an option in the management of patients with back problems. The decision to use opioids should be guided by consideration of their potential complications relative to other options. Patients should be warned about potential physical dependence and the danger associated with the use of opioids while operating heavy equipment or driving. The studies found that patients taking opioid analgesics did not return to full activity sooner than patients taking NSAIDs or acetaminophen. In addition, studies found no difference in pain relief between NSAIDs and opioids. Finally, side effects of opioid analgesics were found to be substantial, including the risk for physical dependence. These side effects are an important concern in conditions that can become chronic, such as back problems. (Bigos, 1999) Pain thresholds are apparently significant lower in chronic whiplash patients than in controls. (Koelbaek, 1999)

From ODG Treatment Integrated Treatment/Disability Duration Guidelines **Pain** (Chronic) (updated 9-8-10) Procedure Summary—Pain:

Zolpidem (Ambien®): Zolpidem is a prescription short-acting nonbenzodiazepine hypnotic, which is approved for the short-term (usually two to six weeks) treatment of insomnia. Proper sleep hygiene is critical to the individual with chronic pain and often is hard to obtain. Various medications may provide short-term benefit. While sleeping pills, so-called minor tranquilizers, and anti-anxiety agents are commonly prescribed in chronic pain, pain specialists rarely, if ever, recommend them for long-term use. They can be habit-forming, and they may impair function and memory more than opioid pain relievers. There is also

concern that they may increase pain and depression over the long-term. ([Feinberg, 2008](#))

NSAIDs (non-steroidal anti-inflammatory drugs)

*Back Pain - Acute low back pain & acute exacerbations of chronic pain:*

Recommended as a second-line treatment after acetaminophen. In general, there is conflicting to negative evidence that NSAIDs are more effective than acetaminophen for acute LBP. ([van Tulder, 2006](#)) ([Hancock, 2007](#)) For patients with acute low back pain with sciatica a recent Cochrane review (including three heterogeneous randomized controlled trials) found no differences in treatment with NSAIDs vs. placebo. In patients with axial low back pain this same review found that NSAIDs were not more effective than acetaminophen for acute low-back pain, and that acetaminophen had fewer side effects. ([Roelofs-Cochrane, 2008](#))

The addition of NSAIDs or spinal manipulative therapy does not appear to increase recovery in patients with acute low back pain over that received with acetaminophen treatment and advice from their physician. ([Hancock, 2007](#))

*Back Pain - Chronic low back pain:* Recommended as an option for short-term symptomatic relief. A Cochrane review of the literature on drug relief for low back pain (LBP) suggested that NSAIDs were no more effective than other drugs such as acetaminophen, narcotic analgesics, and muscle relaxants. The review also found that NSAIDs had more adverse effects than placebo and acetaminophen but fewer effects than muscle relaxants and narcotic analgesics. In addition, evidence from the review suggested that no one NSAID, including COX-2 inhibitors, was clearly more effective than another. [Roelofs-Cochrane, 2008](#)) See also [Anti-inflammatory medications](#).

*Neuropathic pain:* There is inconsistent evidence for the use of these medications to treat long-term neuropathic pain, but they may be useful to treat breakthrough pain and mixed pain conditions such as osteoarthritis (and other nociceptive pain) in patients with neuropathic pain. ([Namaka, 2004](#)) ([Gore, 2006](#))

NSAIDs, GI symptoms & cardiovascular risk

*Use of NSAIDs and SSRIs:* The concurrent use of SSRIs and NSAIDs is associated with moderate excess relative risk of serious upper GI events when compared to NSAIDs alone. This risk was higher for non-selective NSAIDs when compared to Cox-2 selective agents (adjusted odds ratio of 1.77 and 1.33, respectively). ([Helin-Salmivaara, 2007](#)) In particular, it is suggested that in individuals at increased risk for GI bleeding (see above) a consideration be made to switch to an antidepressant with a lower degree of inhibition of serotonin reuptake (Intermediate reuptake: venlafaxine, amitriptyline, imipramine, citalopram; Low reuptake: desipramine, doxepin, trazodone, bupropion, mirtazapine). SSRIs with the highest degree of inhibition of serotonin reuptake

include paroxetine, sertraline, and **fluoxetine**. ([Looper, 2007](#))

NSAIDs, specific drug list & adverse effects

*Meloxicam (Mobic®, generic available): 7.5, 15 mg. Dosing: Osteoarthritis: The usual initial dose is 7.5 mg/day, although some patients may receive additional benefit with an increase to 15 mg a day. The maximum dose is 15 mg/day. Use for mild to moderate pain is off-label. (Mobic® Package Insert) Nabumetone (Relafen®, generic available)*

Opioids for chronic pain

*Recommendations for general conditions:*

- Neuropathic pain: Opioids have been suggested for neuropathic pain that has not responded to first-line recommendations ([antidepressants](#), [anticonvulsants](#)). There are no trials of long-term use. There are virtually no studies of opioids for treatment of chronic lumbar root pain with resultant neuropathy. See [Opioids for neuropathic pain](#).

- Chronic back pain: Appears to be efficacious but limited for short-term pain relief. Longterm efficacy is unclear (>16 weeks), and there is also limited evidence for the use of opioids for chronic low back pain. ([Martell-Annals, 2007](#)) Failure to respond to a time limited course of opioids has led to the suggestion of reassessment and consideration of alternative therapy. There is no evidence to recommend one opioid over another. In patients taking opioids for back pain, the prevalence of lifetime substance use disorders has ranged from 36% to 56% (a statistic limited by poor study design). Limited information indicated that up to one-fourth of patients who receive opioids exhibit aberrant medication-taking behavior. ([Martell-Annals, 2007](#)) ([Chou, 2007](#)) There are three studies comparing Tramadol to placebo that have reported pain relief, but this increase did not necessarily improve function. ([Deshpande, 2007](#)) . . .

*Outcomes measures:* It is now suggested that rather than simply focus on pain severity, improvements in a wide range of outcomes should be evaluated, including measures of functioning, appropriate medication use, and side effects. Measures of pain assessment that allow for evaluation of the efficacy of opioids and whether their use should be maintained include the following: current pain; the least reported pain over the period since last assessment; average pain; intensity of pain after taking the opioid; how long it takes for pain relief; and how long pain relief lasts. ([Nicholas, 2006](#)) ([Ballantyne, 2006](#)) A recent epidemiologic study found that opioid treatment for chronic non- malignant pain did not seem to fulfill any of key outcome goals including pain relief, improved quality of life, and/or improved functional capacity. ([Eriksen, 2006](#))

*Tolerance and addiction:* Opioid tolerance develops with the repeated use of opioids and brings about the need to increase the dose and may lead to sensitization. It is now clear that analgesia may not occur with open-ended

escalation of opioids. It has also become apparent that analgesia is not always sustained over time, and that pain may be improved with weaning of opioids. (Ballantyne, 2006) (Ballantyne, 2003) See [Substance abuse \(tolerance, dependence, addiction\)](#).

## Opioids for neuropathic pain

Not recommended as a first-line therapy. Opioid analgesics and Tramadol have been suggested as a second-line treatment (alone or in combination with first-line drugs). A recent consensus guideline stated that opioids could be considered first-line therapy for the following circumstances: (1) prompt pain relief while titrating a first-line drug; (2) treatment of episodic exacerbations of severe pain; (3) treatment of acute neuropathic pain; & (4) treatment of neuropathic cancer pain. (Dworkin, 2007) Response of neuropathic pain to drugs may differ according to the etiology of therapeutic pain. There is limited assessment of effectiveness of opioids for neuropathic pain, with short-term studies showing contradictory results and intermediate studies (8-70 days) demonstrating efficacy. (Eisenberg-Cochrane, 2006) (Eisenberg-JAMA, 2005) The results of short-term trials were mixed with respect to analgesia (less than 24 hours of treatment). Intermediate trials (average treatment duration of 28 days) showed statistical significance for reducing neuropathic pain by 20% to 30% (and 30% may be the threshold for describing a meaningful reduction of pain).

## Antidepressants for chronic pain

Recommended as a first line option for neuropathic pain, and as a possibility for nonneuropathic pain. (Feuerstein, 1997) (Perrot, 2006) Tricyclics are generally considered a first-line agent unless they are ineffective, poorly tolerated, or contraindicated. Analgesia generally occurs within a few days to a week, whereas antidepressant effect takes longer to occur. (Saarto-Cochrane, 2005) Assessment of treatment efficacy should include not only pain outcomes, but also an evaluation of function, changes in use of other analgesic medication, sleep quality and duration, and psychological assessment. Side effects, including excessive sedation (especially that which would affect work performance) should be assessed. (Additional side effects are listed below for each specific drug.) It is recommended that these outcome measurements should be initiated at one week of treatment with a recommended trial of at least 4 weeks. The optimal duration of treatment is not known because most double-blind trials have been of short duration (6-12 weeks). It has been suggested that if pain is in remission for 3-6 months, a gradual tapering of antidepressants may be undertaken. (Perrot, 2006) (Schnitzer, 2004) (Lin-JAMA, 2003) (Salerno, 2002) (Moulin, 2001) (Fishbain, 2000) (Taylor, 2004) (Gijsman, 2004) (Jick- JAMA, 2004) (Barbui, 2004) (Asnis, 2004) (Stein, 2003) (Pollack, 2003) (Ticknor, 2004) (Staiger, 2003) Long-term effectiveness of anti-depressants has not been established. (Wong, 2007) The effect of this class of medication in combination with other classes of drugs has not been well researched. (Finnerup, 2005) The “number needed to treat” (NNT) methodology (calculated as the reciprocal value of the response rate on active and

placebo) has been used to calculate efficacy of the different classes of antidepressants. (Sindrup, 2005) See also the [Stress/Mental Chapter](#): Antidepressants for the treatment of depression. Also see Comorbid psychiatric disorders.

***Specifically studied underlying pain etiologies:*** (also see below for specific drugs) *Neuropathic pain:* Recommended (tricyclic antidepressants) as a first-line option, especially if pain is accompanied by insomnia, anxiety, or depression. (Saarto-Cochrane, 2007) (ICSI, 2007) Other recent reviews recommended both tricyclic antidepressants and SNRIs (i.e. duloxetine and venlafaxine) as first line options. (Dworkin, 2007) (Finnerup, 2007)

*Non-neuropathic pain:* Recommended as an option in depressed patients, but effectiveness is limited. Non-neuropathic pain is generally treated with analgesics and antiinflammatories.

In guidelines for painful rheumatic conditions recommended by Perrot, it was suggested that antidepressants may be prescribed as analgesics in non-depressed patients, with the first-line choice being tricyclics initiated at a low dose, increasing to a maximally tolerated dose. (Perrot, 2006)

Anti-epilepsy drugs (AEDs) for pain

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

Recommended for neuropathic pain (pain due to nerve damage), but not for acute nociceptive pain (including somatic pain). (Gilron, 2006) (Wolfe, 2004) (Washington, 2005) (ICSI, 2005) (Wiffen-Cochrane, 2005) (Attal, 2006) (Wiffen-Cochrane, 2007) (Gilron, 2007) (ICSI, 2007) (Finnerup, 2007)

There is a lack of expert consensus on the treatment of neuropathic pain in general due to heterogeneous etiologies, symptoms, physical signs and mechanisms. Most randomized controlled trials (RCTs) for the use of this class of medication for neuropathic pain have been directed at postherpetic neuralgia and painful polyneuropathy (with diabetic polyneuropathy being the most common example). There are few RCTs directed at central pain and none for painful radiculopathy. (Attal, 2006) The choice of specific agents reviewed below will depend on the balance between effectiveness and adverse reactions. See also specific drug listings below:

[Gabapentin](#) (Neurontin®); [Pregabalin](#) (Lyrica®); [Lamotrigine](#) (Lamictal®); [Carbamazepine](#) (Tegretol®); [Oxcarbazepine](#) (Trileptal®); [Phenytoin](#) (Dilantin®); [Topiramate](#) (Topamax®); [Levetiracetam](#) (Keppra®); [Zonisamide](#) (Zonegran®); & [Tiagabine](#) (Gabitril®)

*Outcomes:* A “good” response to the use of AEDs has been defined as a 50% reduction in pain and a “moderate” response as a 30% reduction. It has been reported that a 30% reduction in pain is clinically important to patients and a lack

of response of this magnitude may be the “trigger” for the following: (1) a switch to a different first-line agent (TCA, SNRI or AED are considered first-line treatment); or (2) combination therapy if treatment with a single drug agent fails. (Eisenberg, 2007) (Jensen, 2006) After initiation of treatment there should be documentation of pain relief and improvement in function as well as documentation of side effects incurred with use. The continued use of AEDs depends on improved outcomes versus tolerability of adverse effects. AEDs are associated with teratogenicity, so they must be used with caution in woman of childbearing age.

Preconception counseling is recommended for anticonvulsants (due to reductions in the efficacy of birth control pills). (Clinical Pharmacology, 2008)

Manufacturers of antiepileptic drugs will need to add a warning to their labeling indicating that use of the drugs increases risk for suicidal thoughts and behaviors, according to an FDA Alert issued December 16. (FDA MedWatch, 2008)

**Pregabalin (Lyrica®, no generic available)** has been documented to be effective in treatment of diabetic neuropathy and postherpetic neuralgia, has FDA approval for both indications, and is considered first-line treatment for both. This medication is designated as a Schedule V controlled substance because of its causal relationship with euphoria. (Blommel, 2007) This medication also has an anti-anxiety effect. Pregabalin is being considered by the FDA as treatment for generalized anxiety disorder and social anxiety disorder. In June 2007 the FDA announced the approval of pregabalin as the first approved treatment for fibromyalgia. (ICSI, 2007) (Tassone, 2007) (Knotkova, 2007) (Eisenberg, 2007) (Crofford, 2005) (Stacey, 2008) Dose adjustment is necessary in patients with renal insufficiency. The antiepileptic agents gabapentin and pregabalin have attained widespread usage in the treatment of painful diabetic peripheral neuropathy (DPN). This pooled analysis of 7 randomized controlled trials comparing different doses and frequencies of pregabalin for painful DPN concluded that pregabalin at doses of 150, 300, and 600 mg daily is associated with dose-related relief of pain and reduction in sleep interference in patients with painful DPN. (Freeman, 2008)

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