

# INDEPENDENT REVIEWERS OF TEXAS, INC.

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**[Date notice sent to all parties]:**

**06/30/2015**

**IRO CASE #:**

**DESCRIPTION OF THE SERVICE OR SERVICES IN DISPUTE: Duloxetine, Gralise, norco 10 325 mg**

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

Board Certified PM&R; Board Certified Pain Medicine

**REVIEW OUTCOME:**

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

Upheld (Agree)

Provide a description of the review outcome that clearly states whether medical necessity exists for each of the health care services in dispute.

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

The patient is a male who initially presented on xx/xx/xx with a left ankle fracture. The peer review dated 06/13/13 indicates the patient having developed post-traumatic arthritis. There is an indication the patient had also sustained a pilon fracture at the left ankle resulting in an ORIF as well as subsequent multiple surgeries. An acromion fracture was also identified which was addressed with an ORIF. The patient had responded well to physical therapy. There is an indication the patient had undergone physical therapy and was subsequently discharged on 05/28/13. The note indicates the patient utilizing Motrin, Flexeril, and Vicodin for pain relief. The peer review dated 06/26/14 indicates the patient continuing with the use of Hydrocodone, Gabapentin, Ibuprofen, and Cyclobenzaprine. The note indicates the patient being recommended to discontinue the use of Cyclobenzaprine. X-rays of the left ankle and foot revealed a callous formation at the fracture site. The note indicates the patient able to demonstrate 0 degrees of extension, 35 degrees of flexion, 15 degrees of inversion, and 5 degrees of eversion. The patient had been prescribed the use of Cymbalta, Gralise, and Norco at that time. Upon exam, mild loss of sensation was identified at the dorsum of the left foot. The clinical note dated 10/15/14 indicates the patient continuing with 4/10 pain. The note indicates the patient able to complete his activities of daily living. No issues with his sleep hygiene were identified. Upon exam, allodynia was identified at the left foot. Decreased temperatures were also identified as well. The clinical note dated 12/08/14 indicates the patient continuing with left lower extremity pain. The patient was continuing with the use of Gabapentin as well as Norco.

The utilization reviews dated 03/31/15 and 05/13/15 resulted in denials as insufficient information had been provided confirming the need for the prescribed drug regimen.

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

The documentation indicates the patient having sustained a left ankle fracture with subsequent findings consistent with CRPS, manifested by allodynia and temperature changes. The use of Duloxetine is indicated for patients with neuropathic related pain. Given the ongoing findings consistent with CRPS, it would be reasonable for the patient to be medicated with the use of Duloxetine. Therefore, the request for the Duloxetine is recommended for certification. However, Gralise is recommended for patients with findings consistent with restless leg syndrome. No information was submitted regarding the patient's findings regarding any symptoms associated with RLS. Therefore, this request is not indicated as medically necessary. The documentation indicates the patient having been prescribed the use of Norco for a prolonged period of time. Given the ongoing use of opioids, it would be reasonable for the patient to undergo periodic and unscheduled urine drug screens. However, no urine drug screens were submitted for review. Additionally, the continued use of opioids is recommended for patients where a significant reduction in pain along with an objective functional improvement is documented. No information was submitted regarding the patient's significant reduction in pain specifically attributable to the use of this medication. Additionally, no information was submitted regarding an objective functional improvement. Therefore, the continued use of this medication is not fully indicated. Given the prolonged use of opioid therapy, it would be reasonable for the patient to undergo a weaning process from this medication. As such, it is the opinion of this reviewer that the request for the use of Duloxetine is recommended as medically necessary given the patient's findings consistent with CRPS; however, the continued use of Gralise and Norco 10/325mg is not recommended as medically necessary.

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

**MEDICAL JUDGEMENT, CLINICAL EXPERIENCE, AND EXPERTISE IN ACCORDANCE WITH ACCEPTED MEDICAL STANDARDS**

**ODG- OFFICIAL DISABILITY GUIDELINES & TREATMENT GUIDELINES**

Duloxetine (Cymbalta®)

Recommended as an option in first-line treatment of neuropathic pain. Duloxetine (Cymbalta®) is a norepinephrine and serotonin reuptake inhibitor antidepressant (SNRIs). It has FDA approval for treatment of depression, generalized anxiety disorder, and for the treatment of pain related to diabetic neuropathy, with effect found to be significant by the end of week 1 (effect measured as a 30% reduction in baseline pain). The starting dose is 20-60 mg/day, and no advantage has been found by increasing the dose to twice a day, except in fibromyalgia. The medication has been found to be effective for treating fibromyalgia in women with and without depression, 60 mg once or twice daily. (Arnold, 2005) The most frequent side effects include nausea, dizziness and fatigue. GI symptoms are more common early in treatment. The side effect profile of Duloxetine is thought to be less bothersome to patients than that of tricyclic antidepressants. Note: On October 17, 2005, Eli Lilly and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revision to the PRECAUTIONS/Hepatotoxicity section of the prescribing information for Cymbalta. Postmarketing reports of hepatic injury (including hepatitis and cholestatic jaundice) suggest that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. The new labeling extends the Precaution against using Cymbalta in patients with substantial alcohol use to include those patients with chronic liver disease. It is recommended

that Cymbalta not be administered to patients with hepatic insufficiency. See the Stress Chapter for more information and references. See Antidepressants for chronic pain for general guidelines, as well as specific Duloxetine listing for more information and references. On June 13, 2008, the FDA approved a new indication for duloxetine HCl delayed-release capsules (Cymbalta®; Eli Lilly and Company) for the management of fibromyalgia in adults. The FDA notes that although duloxetine was effective for reducing pain in patients with and without major depressive disorder, the degree of pain relief may have been greater in those with comorbid depression. Treatment of fibromyalgia with duloxetine should be initiated at 30 mg/day for 1 week and then uptitrated to the recommended 60-mg dose. (Waknine, 2008) Note: This drug was recently included in a list of 20 medications identified by the FDA's Adverse Event Reporting System, that are under FDA investigation. (FDA, 2008) An FDA panel concluded that Cymbalta was effective in treating chronic low back pain, and they voted in favor of Eli Lilly's request to broaden the indication to include the treatment of chronic pain. (FDA, 2010) On November 4, 2010, the FDA approved duloxetine HCl delayed-release capsules (Cymbalta; Eli Lilly and Co) for the once-daily treatment of chronic musculoskeletal pain. Regulatory approval followed a positive vote regarding the use of duloxetine to treat chronic low back pain, but the committee did not express the same confidence in the drug's usefulness as a treatment for osteoarthritis. Despite this, duloxetine has been approved for both chronic low back pain and osteoarthritis. The recommended dose is 60 mg daily. Duloxetine delayed-release capsules previously were approved for the treatment of major depressive disorder, generalized anxiety disorder, diabetic peripheral neuropathic pain, and fibromyalgia. (FDA, 2010) According to an AHRQ Comparative Effectiveness Review, sparse, low-strength evidence suggests that duloxetine effects on global improvement (PGI-I) and fibromyalgia impact (FIQ) do not differ in the MDD patient subgroup. (Forte, 2015)

#### Gralise (gabapentin enacarbil ER)

Not recommended. See the Knee Chapter, where Gralise is addressed, and it is not recommended as a first-line agent for restless legs syndrome. There is no evidence to support use of Gralise for neuropathic pain conditions or fibromyalgia without a trial of generic gabapentin regular release.

#### Opioids

Opioids, criteria for use

#### CRITERIA FOR USE OF OPIOIDS

##### Therapeutic Trial of Opioids

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

- (a) Are there reasonable alternatives to treatment, and have these been tried?
- (b) Is the patient likely to improve? Examples: Was there improvement on opioid treatment in the acute and subacute phases? Were there trials of other treatment, including non-opioid medications?
- (c) Has the patient received a screen for the risk of addiction? Is there likelihood of abuse or an adverse outcome? Specific questions about current use of alcohol, illegal drugs, other prescription drugs, and over-the-counter drugs should be asked.

Obtaining a history of personal and/or family substance abuse issues is important. See Substance abuse (tolerance, dependence, addiction). See Opioids, screening for risk of addiction. (Webster, 2008) (Ballyantyne, 2007)

(d) Ask about Red Flags indicating that opioids may not be helpful in the chronic phase: (1) Little or no relief with opioid therapy in the acute and subacute phases. (2) The patient has been given a diagnosis in one of the particular diagnostic categories that have not been shown to have good success with opioid therapy: conversion disorder; somatization disorder; pain disorder associated with psychological factors (such as anxiety or depression, or a previous history of substance abuse). Patients may misuse opioids prescribed for pain to obtain relief from depressed feelings, anxiety, insomnia, or discomforting memories. There are better treatments for this type of pathology. (Sullivan, 2006) (Sullivan, 2005) (Wilsey, 2008) (Savage, 2008)

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

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

(a) Attempt to determine if the pain is nociceptive or neuropathic. Also attempt to determine if there are underlying contributing psychological issues. Neuropathic pain may require higher doses of opioids, and opioids are not generally recommended as a first-line therapy for some neuropathic pain.

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

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

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

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

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

(g) The patient should have at least one physical and psychosocial assessment by the treating doctor (and a possible second opinion by a specialist) to assess whether a trial of opioids should occur. When subjective complaints do not correlate with imaging studies and/or physical findings and/or when psychosocial issue concerns exist, a second opinion with a pain specialist and a psychological assessment should be obtained. (Sullivan, 2006) (Sullivan, 2005) (Wilsey, 2008) (Savage, 2008) (Ballyantyne, 2007)

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

(i) A written consent or pain agreement for chronic use is not required but may make it easier for the physician and surgeon to document patient education, the treatment plan, and the informed consent. Patient, guardian, and caregiver attitudes about

medicines may influence the patient's use of medications for relief from pain. See Guidelines for Pain Treatment Agreement. This should include the consequences of non-adherence.

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

### 3) Initiating Therapy

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

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

(c) Only change 1 drug at a time.

(d) Prophylactic treatment of constipation should be initiated.

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

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

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

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

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

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

(e) Use of drug screening or inpatient treatment with issues of abuse, addiction, or poor pain control. (Webster, 2008)

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

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

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

depression, anxiety or irritability. Consider an addiction medicine consult if there is evidence of substance misuse. (Sullivan, 2006) (Sullivan, 2005) (Wilsey, 2008) (Savage, 2008) (Ballyantyne, 2007)

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

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

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

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

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

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

(b) Continuing pain with the evidence of intolerable adverse effects; lack of significant benefit (persistent pain and lack of improved function despite high doses of opiates- e.g. > 120 mg/day morphine equivalents)

(c) Decrease in functioning

(d) Resolution of pain

(e) If serious non-adherence is occurring

(f) The patient requests discontinuing

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

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

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

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

(k) Routine long-term opioid therapy is not recommended, and ODG recommends

consideration of a one-month limit on opioids for new chronic non-malignant pain patients in most cases, as there is little research to support use. The research available does not support overall general effectiveness and indicates numerous adverse effects with long-term use. The latter includes the risk of ongoing psychological dependence with difficulty weaning. See Opioids for chronic pain.

#### 7) When to Continue Opioids

- (a) If the patient has returned to work
- (b) If the patient has improved functioning and pain