



Specialty Independent Review Organization

## Notice of Independent Review Decision

**DATE OF REVIEW:** 3/11/2008

**IRO CASE #:**

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

The item in dispute is the prospective medical necessity of the prescription drug, Cymbalta.

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

The reviewer is a board certified physical medicine and rehabilitation physician with greater than 10 years of experience in this field.

**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)

The reviewer disagrees with the previous adverse determination regarding the prospective medical necessity of the prescription drug, Cymbalta.

**INFORMATION PROVIDED TO THE IRO FOR REVIEW**

Records were received and reviewed from the following parties:

MD  
DO

These records consist of the following (duplicate records are only listed from one source): Records from: MD exam report-1/1/07; EOBs for dates of service 7/30/07-10/30/07; Print notes-12/5/07-7/16/07; denial letter-2/26/08. Records from MD: Follow-up Visit notes-10/30/07-3/10/06 and Dr. reconsideration letter.

Records from DO: Dr. DDE report-5/31/07 & 9/2/2000; DWC69-5/31/07;  
TWCC69-9/5/2000

A copy of the Official Disability Guidelines was not provided for this review.

**PATIENT CLINICAL HISTORY [SUMMARY]:**

The patient injured his cervical spine by repeatedly reaching overhead. An MRI verified DDD. An EMG verified CTS and ulnar neuropathy of the right. He has been managed with analgesic medications, NSAIDs, sedative, and muscle relaxants. Interventions have included TrP injections, ESI (20-30% relief per PA-C on 6/23/2006), and facet blocks. Rhizotomy has been proposed. Per Dr. on 10/30/2007 the patient has right sided arm pain along the right C7 distribution. He is prescribing Cymbalta for pain and secondary anxiety and depression. The prescription of Cymbalta is under dispute. Dr. is of the opinion that his medication is not indicated as this type of medication is not indicated specifically for a soft tissue injury. He is of the opinion that the injury is limited to a soft tissue injury of the cervical spine. There is no reference to the Official Disability Guidelines in his report.

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

The reviewer cites the ODG:

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. 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. Post marketing 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.

Recommended as a first line option for neuropathic pain, and as a possibility for non-neuropathic pain. 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. (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.

**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. A switch to a mixed action agent is generally only recommended if tricyclics are ineffective, poorly tolerated, or contraindicated. 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 anti-inflammatories. In guidelines recommended by Perrot, it was suggested that antidepressants may be prescribed as analgesics in non-depressed patients, with the first-line choice being tricyclics initiated at a low dose, increasing to a maximally tolerated dose. They also suggested that trials of newer classes of antidepressants should only be initiated if tricyclics proved to be ineffective, if the patient was unable to tolerate side effects, or they were contraindicated.

**Selective serotonin and norepinephrine reuptake inhibitors (SNRIs):**

**Duloxetine (Cymbalta®):** FDA-approved for anxiety, depression, and diabetic neuropathy. Used off-label for fibromyalgia and neuropathic pain. Duloxetine is recommended as a first-line option for diabetic neuropathy.

*Side effects:* CNS: dizziness, fatigue, somnolence, drowsiness, anxiety (3% vs. 2% for placebo), insomnia (8-13% vs. 6-7% for placebo). GI: nausea and vomiting (5-30%), weight loss (2%). Duloxetine can worsen diabetic control in some patients. It also causes sexual dysfunction. (Maizels, 2005)

*Dosing:* 60 mg once a day as an off-label option for chronic pain syndromes. Dosage adjustment may be required in patients with renal insufficiency.

Venlafaxine (Effexor®): FDA-approved for anxiety, depression, panic disorder and social phobias. Off-label use for fibromyalgia, neuropathic pain, and diabetic neuropathy.

*Dosing: Neuropathic pain (off-label indication):* 37.5 mg once daily, increase by 37.5 mg per week up to 300 mg daily. (Maizels, 2005) (ICSI, 2007) *Trial period:* Some relief may occur in first two weeks; full benefit may not occur until six weeks.

Dr. documents that the patient is prescribing Cymbalta for pain and secondary anxiety and depression. The prescription of Cymbalta is under dispute. The ODG supports the prescription of this medicine for neuropathic pain, anxiety, and depression. The patient's injury is not limited to a soft tissue injury of the cervical spine. He has a chronic pain syndrome with secondary depression/anxiety as well as component of neuropathic pain. Therefore the proposed prescription is medically necessary.

**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**
- 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)**