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**Notice of Independent Review Decision**

**Date notice sent to all parties:**

October 2, 2013

**IRO CASE #:**

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

Topical compound including Ketamine, Baclofen, Cyclobenzaprine, Diclofenac, Gabapentin, Orphenadrine, Tetracaine, and Lipoderm base cream.

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

Board Certified Neurology

**REVIEW OUTCOME:**

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

Overturned (Disagree)

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

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

Clinical report dated 06/04/04  
Laboratory results dated 09/03/13 – 09/12/13  
Clinical reports dated 08/24/11 – 08/23/13  
Radiographs skeletal survey dated 09/05/13  
Procedure report dated 09/04/13  
Medication list as of 09/19/13  
Letters from patient's wife dated 02/25/13 - 09/18/13  
Letter dated 03/28/13  
Request for reconsideration from the patient's wife dated 07/26/12  
Prior utilization reviews

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

The patient is a male who sustained an injury on xx/xx/xx. It appears the patient was involved in a motor vehicle accident that resulted in a traumatic brain injury. The patient has been followed for an extensive period of chronic pain management. As of August of 2011, the patient was found to have some remaining neurocognitive issues and there were recommendations for medication regimen simplification. As of August of 2011, the patient's list of medications was extensive. It is noted the patient was utilizing multiple narcotic medications including Percocet and Methadone as well as several topical medications to include Lidocaine and Polyethylene Glycol. The patient was noted to have been recommended for a compounded medication cream in January of 2012 to reduce toxicity from 'Caine medications. The clinical report from 04/09/12 indicates that the patient's compounded medication cream has provided benefits. The patient continued to report radiating pain in the inner thigh and into the left lower extremity. The patient was able to simplify his drug regimen as recommended. The patient was recommended to continue with the compounded topical medication. The most recent evaluation on 08/23/13 stated the patient continued to have worsening weakness in the upper extremities. The patient denied any side effects from current medication regimens. There were again indications that the compounded medication was beneficial for this patient. As of 09/19/13, the patient's medications were still extensive. The patient continued to utilize Clonazepam, Percocet, Seroquel, Cymbalta, as well as the compounded topical medication for his symptoms.

The compounded medication in question was denied by utilization review as there was insufficient evidence within clinical literature to establish the efficacy of topical compounded medications that included medications not approved by the FDA for transdermal use to include Ketamine, Baclofen, Cyclobenzaprine, Gabapentin, and Orphenadrine.

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

This patient has been followed for ongoing complaints of chronic pain in the extremities following a motor vehicle accident from xxxx. The patient is noted to have sustained a traumatic brain injury as a result of the accident. The patient has been able to successfully simplify his extensive medication list and the clinical documentation reported good effects from the compounded medication being provided. Although the clinical literature regarding topical compounded medications is limited, there are indications for use of topical medications to include the intolerance or contraindications to oral formulations. In this case, the patient is reasonably an outlier to Official Disability Guidelines recommendations regarding topical compounded medications. The patient has been able to reduce and simplify his extensive medication list and this topical medication does provide a significant amount of benefit in regards to subjective complaints. Due to the simplification of

the medication list as a result of the use of this compounded medication, it is this reviewer's opinion that medical necessity for ongoing use of compounded Ketamine, Baclofen, Cyclobenzaprine, Diclofenac, Gabapentin, Orphenadrine, Tetracaine, and Lipoderm is established.

**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**

Topical Analgesics

Recommended as an option as indicated below. Largely experimental in use with few randomized controlled trials to determine efficacy or safety. Primarily recommended for neuropathic pain when trials of antidepressants and anticonvulsants have failed. (Namaka, 2004) These agents are applied locally to painful areas with advantages that include lack of systemic side effects, absence of drug interactions, and no need to titrate. (Colombo, 2006) Many agents are compounded as monotherapy or in combination for pain control (including NSAIDs, opioids, capsaicin, local anesthetics, antidepressants, glutamate receptor antagonists,  $\alpha$ -adrenergic receptor agonist, adenosine, cannabinoids, cholinergic receptor agonists,  $\gamma$  agonists, prostanoids, bradykinin, adenosine triphosphate, biogenic amines, and nerve growth factor). (Argoff, 2006) There is little to no research to support the use of many of these agents. *Any compounded product that contains at least one drug (or drug class) that is not recommended is not recommended.* The use of these compounded agents requires knowledge of the specific analgesic effect of each agent and how it will be useful for the specific therapeutic goal required. [Note: Topical analgesics work locally underneath the skin where they are applied. These do not include transdermal analgesics that are systemic agents entering the body through a transdermal means. See Duragesic® (fentanyl transdermal system).]

*Non-steroidal antiinflammatory agents (NSAIDs):* The efficacy in clinical trials for this treatment modality has been inconsistent and most studies are small and of short duration. Topical NSAIDs have been shown in meta-analysis to be superior to placebo during the first 2 weeks of treatment for osteoarthritis, but either not afterward, or with a diminishing effect over another 2-week period. (Lin, 2004) (Bjordal, 2007) (Mason, 2004) When investigated specifically for osteoarthritis of the knee, topical NSAIDs have been shown to be superior to placebo for 4 to 12 weeks. In this study the effect appeared to diminish over time and it was stated that further research was required to determine if results were similar for all preparations. (Biswal, 2006) These medications may be useful for chronic musculoskeletal pain, but there are no long-term studies of their effectiveness or safety. (Mason, 2004) *Indications: Osteoarthritis and tendinitis, in particular, that of the knee and elbow or other joints that are amenable to topical treatment:* Recommended for short-term use (4-12 weeks). There is little evidence to utilize topical NSAIDs for treatment of osteoarthritis of the

spine, hip or shoulder.

*Neuropathic pain:* Not recommended as there is no evidence to support use. *FDA-approved agents:*

*Voltaren® Gel 1% (diclofenac):* Indicated for relief of osteoarthritis pain in joints that lend themselves to topical treatment (ankle, elbow, foot, hand, knee, and wrist). It has not been evaluated for treatment of the spine, hip or shoulder. Maximum dose should not exceed 32 g per day (8 g per joint per day in the upper extremity and 16 g per joint per day in the lower extremity). The most common adverse reactions were dermatitis and pruritus. (Voltaren® package insert) For additional adverse effects: See NSAIDs, GI symptoms and cardiovascular risk; & NSAIDs, hypertension and renal function.

*Non FDA-approved agents: Ketoprofen:* This agent is not currently FDA approved for a topical application. It has an extremely high incidence of photocontact dermatitis. (Diaz, 2006) (Hindsen, 2006) Absorption of the drug depends on the base it is delivered in. (Gurol, 1996). Topical treatment can result in blood concentrations and systemic effect comparable to those from oral forms, and caution should be used for patients at risk, including those with renal failure. (Krummel 2000)

*Capsaicin:* Recommended only as an option in patients who have not responded or are intolerant to other treatments. *Formulations:* Capsaicin is generally available as a 0.025% formulation (as a treatment for osteoarthritis) and a 0.075% formulation (primarily studied for post-herpetic neuralgia, diabetic neuropathy and post-mastectomy pain). There have been no studies of a 0.0375% formulation of capsaicin and there is no current indication that this increase over a 0.025% formulation would provide any further efficacy. *Indications:* There are positive randomized studies with capsaicin cream in patients with osteoarthritis, fibromyalgia, and chronic non-specific back pain, but it should be considered experimental in very high doses. Although topical capsaicin has moderate to poor efficacy, it may be particularly useful (alone or in conjunction with other modalities) in patients whose pain has not been controlled successfully with conventional therapy. The number needed to treat in musculoskeletal conditions was 8.1. The number needed to treat for neuropathic conditions was 5.7. (Robbins, 2000) (Keitel, 2001) (Mason-BMJ, 2004) See also Capsaicin.

*Baclofen:* Not recommended. There is currently one Phase III study of Baclofen-Amitriptyline-Ketamine gel in cancer patients for treatment of chemotherapy-induced peripheral neuropathy.

There is no peer-reviewed literature to support the use of topical baclofen.

*Other muscle relaxants:* There is no evidence for use of any other muscle relaxant as a topical product.

### **Compound drugs**

Not recommended as a first-line therapy for most patients, but recommended as an option after a

trial of first-line FDA-approved drugs, if the compound drug uses FDA-approved ingredients that are recommended in ODG. ([Wynn, 2011](#)) See specific entries for each ingredient. See also [Topical analgesics, compounded](#). In general, FDA-approved drugs should be tried prior to prescribing a compound drug, unless specific patient issues with any appropriate FDA-approved drugs have already been identified. Pharmacy compounding has traditionally involved combining drug ingredients to meet the needs of specific patients for medications that are not otherwise commercially available, and it is undertaken on a patient-by-patient basis for patients who, for example, might be allergic to inactive ingredients in FDA-approved drugs or may need a different dosage strength or route of administration. Unlike commercially available drugs, these products are not approved by the FDA but rather are regulated by the state pharmacy board and state law governing the practice of pharmacy. The FDA does not regulate pharmacy-compounded products in recognition of the important public health function performed by traditional compounding. Recently, some pharmacies have been making and marketing stock compound drugs for the WC patient population. Among the FDA "Red Flags" for Enforcement Action on Compounded Drugs is: "Compounding drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to amounts compounded after receiving valid prescriptions." ([FDA, 2011](#)) Compound topical analgesics may provide relief by acting locally over the painful site with lower risk of systemic adverse effects on the gastrointestinal system and drug interactions than oral NSAIDs. The issues surrounding compound drugs are due to uncertainties regarding whether the products are medically appropriate and whether payments are reasonable, with the latter issue possibly also involving who dispenses the drug. Medical necessity should be based on the patient's needs combined with the medical and scientific evidence presented in ODG. ODG does not address pricing and fee schedules, but in general there should be consistency within a pharmacy fee schedule for products containing the same active ingredients, so that there is not an inappropriate incentive to use compounding. ([Wynn, 2011](#)) See also [Co-pack drugs](#); [Medical foods](#); [Physician-dispensed drugs](#); [Repackaged drugs](#); & [Topical analgesics, compounded](#).

Criteria for Compound drugs:

- (1) Include at least one drug substance (or active ingredient) that is the sole active ingredient in an FDA-approved prescription drug, not including OTC drugs.
- (2) Include only bulk ingredients that are components of FDA-approved drugs that have been made in an FDA-registered facility and have an NDC code.
- (3) Is not a drug that was withdrawn or removed from the market for safety reasons.
- (4) Is not a copy of a commercially available FDA-approved drug product.
- (5) Include only drug substances that have been supported as safe and effective for the prescribed indication by the FDA-approval process and/or by adequate medical and scientific evidence in the medical literature. This would allow off-label usage when supported by medical evidence. See specific entries for each ingredient in ODG for the medical and scientific evidence. See also [Topical analgesics, compounded](#). ([Wynn, 2011](#))