

Notice of Independent Review Decision

April 5, 2013

IRO CASE #:

DESCRIPTION OF THE SERVICE OR SERVICES IN DISPUTE:

Medical Necessity: 3 Refills for Compound Ket + Bac + Cyclo + Diclo + Gab + Orph + Tetra + Lopderm Plo Base D9630

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

The physician providing this review is Board Certified, American Board of PM/Occupational Medicine. This reviewer's primary practice is in the area of occupational environmental medicine. The physician is in active practice and has hospital privileges in the state of Texas.

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 medical necessity exists for each of the health care services in dispute.

Upon independent review, the physician finds that the previous adverse determination should be Upheld.

INFORMATION PROVIDED TO THE IRO FOR REVIEW:

Records Received: 17 page fax 03/18/13 Texas Department of Insurance IRO request, 31 pages of documents received via fax on 03/19/13 URA response to disputed services including administrative and medical. Dates of documents range from xx/xx/xx (DOI) to 03/18/13.



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PATIENT CLINICAL HISTORY [SUMMARY]:

Male patient TLT, was treated on or about 10/12/12 and was prescribed compounded cream Ket (ketamine) + Bac (baclofen) + Cyclo (cyclobenzaprine) + Diclo (diclofenac) + Gab (gabapentin) + Orph (orphenadrine) + Tetra (tetracaine) + Lipoderm PLO base. This is a pain cream and he was given three refills. There were no other clinical records submitted in support of this prescription. A case review from The Hartford states the claimant was injured on xx/xx/xx in a motor vehicle accident (he was broadsided by an 18 wheeler). He has multiple medical problems including a traumatic brain injury. An MRI of the right shoulder revealed marked tendinosis with a possible full thickness tear. He is taking multiple medications. He has right shoulder pain that has responded to steroid shots. The use of topical cream was denied. An appeal states that the patient had been using this cream for some time and he described pain relief. The cream was again denied.

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

The history and documentation do not objectively support the request for the use of the compounded cream Ket (ketamine) + Bac (baclofen) + Cyclo (cyclobenzaprine) + Diclo (diclofenac) + Gab (gabapentin) + Orph (orphenadrine) + Tetra (tetracaine) + Lipoderm PLO base. It appears that the claimant is using it for his right shoulder. The Official Disability Guidelines 2013 state topical diclofenac, gabapentin, and cyclobenzaprine and other muscle relaxants are not recommended. Ketamine is under study. Lidocaine is only recommended in the form of Lidoderm and tetracaine and orphenadrine are not mentioned. Topical salicylates are the only creams/lotions supported by the ODG. Topical muscle relaxants are not addressed by the ODG. However, it is not clear why the claimant requires this type of medication as no evidence of muscle spasm has been submitted.

The claimant's use of multiple other medication is not described, including possible intolerance/side effects or lack of efficacy. Of note, the ODG further state "any compounded product that contains at least one drug (or drug class) that is not recommended is not recommended." The medical necessity of this compounded cream has not been clearly demonstrated.

Official Disability Guidelines, 2013. Formulary and Pain Chapter:

Topical analgesics may be recommended as an option [but are] argely 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



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are compounded as monotherapy or in combination for pain control (including NSAIDs, opioids, capsaicin, local anesthetics, antidepressants, glutamate receptor antagonists, α -adrenergic receptor agonist, adenosine, cannabinoids, cholinergic receptor agonists, γ 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 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. For example, see Duragesic® (fentanyl transdermal system).]

Non-steroidal anti-inflammatory agents (NSAIDs): Recommended for the following indications:

Acute pain: Recommended for short-term use (one to two weeks), particularly for soft tissue injuries such as sprain/strains. According to a recent review, topical NSAIDs can provide good levels of pain relief for sprains, strains, and overuse injuries, with the advantage of limited risk of systemic adverse effects as compared to those produced by oral NSAIDs. They are considered particularly useful for individuals unable to tolerate oral administration, or for whom it is contraindicated. There appears to be little difference in analgesic efficacy between topical diclofenac, ibuprofen, ketoprofen and piroxicam, but indomethacin is less effective, and benzydamine is no better than placebo. The number needed to treat for clinical success, defined as 50% pain relief, for all topical NSAIDs combined vs. placebo was 4.5 (95% confidence interval [CI], 3.9 - 5.3) for treatment periods of 6 to 14 days. Current studies indicate 6 or 7 out of 10 patients have effective pain control with topical agents vs. 4 out of 10 with placebo. The reason for the high placebo rate is that most sprain/strain injuries improve on their own. (Massey, 2010) (Mason, 2004)

Osteoarthritis and tendinitis, in particular, that of the knee, elbow, and hand or other joints that are amenable to topical treatment: Recommended for short-term use (4-12 weeks). (See also the Knee Chapter.) (Underwood, 2008) (Mason, 2004) (Biswal, 2006) (Green, 2002) (Niethard, 2005) (Conaghan, 2008) (Altman, 2009) (Wenham, 2010) (Zhang, 2007) (NICE, 2008) (Zhang, 2010) (Altman, 2011) The American Academy of Orthopedic Surgeons recommends topical NSAIDs if there is increased GI risk with use of NSAIDs as one option for treatment. (Richmond, 2010) There are no studies evaluating topical ketoprofen for treatment of hand osteoarthritis. Topical ketoprofen gel has been compared to oral celecoxib, with WOMAC physical function scores significant for the later but not the topical treatment. (Rother, 2007)

Osteoarthritis of the hip and shoulder: There is little evidence to utilize topical NSAIDs for treatment of osteoarthritis of the hip or shoulder.

Osteoarthritis of the low back: There is no evidence to recommend a NSAID dosage form other than an oral formulation for low back pain. (Roelofs, 2008) (Haroutianian, 2010)

Widespread musculoskeletal pain: Not recommended.

Neuropathic pain: Not recommended as there is no evidence to support use. (Haroutianian, 2010) (Finnerup, 2005)

General information: The theory behind using a topical NSAID is to achieve a therapeutic concentration in the tissue adjacent to the application, allowing for safe serum concentration. This would allow for less adverse GI events, eliminate first-pass metabolism and reduce risk of other GI events associated with higher systemic doses provided with oral formulations. Overall, a high concentration of drug is observed in the dermis and muscles (equivalent to that obtained orally), with less gastrointestinal effect. Plasma concentrations are 5% to 15% of those achieved systemically. (Kienzler, 2010) Topically applied NSAIDs appear to reach the synovial fluid of joints, although the mechanism for delivery remains unclear. 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-



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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. The effect appeared to diminish over time and it was stated that further research is 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. In terms of acute pain, topical NSAIDs were found to produce a 50% reduction in pain at one week, with the most significant results obtained with use of ketoprofen, while indomethacin was barely distinguished from placebo. (Mason, 2004)

Pharmacokinetics and systemic availability: Absorption and penetration through the skin depends on the active medication, formulation (i.e. gel vs. solution), carrier-medicated transport, and penetration enhancement. Each of these differences produces differences in systemic levels attained. The carrier may also contribute to toxicity. Toxicity by dose has not been established (especially for trials that allowed for more than one joint to be treated). Excessive amounts of topical NSAID may produce higher than desired levels, hindering the advantage of a topical formulation. (Haroutiunian, 2010) (Kienzler, 2010)

Compounded formulations: There is little research available in terms of bioavailability and objective clinical endpoints for these agents. (Haroutiunian, 2010)

FDA-approved agents: At this time, the only available FDA-approved topical NSAID is diclofenac. Voltaren® Gel 1% (diclofenac): Indicated for relief of osteoarthritis pain in a joint that lends itself 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) Clinical trial data suggest that diclofenac sodium gel (the first topical NSAID approved in the US) provides clinically meaningful analgesia in OA patients with a low incidence of systemic adverse events. (Altman, 2009) The labeling for topical diclofenac has been updated to warn about drug-induced hepatotoxicity. (FDA, 2009) Voltaren Gel was effective in adults regardless of age. Treatment-related application site dermatitis was more common with Voltaren Gel, but gastrointestinal AEs were infrequent. It is recommended for osteoarthritis after failure of an oral NSAID, or contraindications to oral NSAIDs, or for patients who cannot swallow solid oral dosage forms. (Baraf, 2011) (Kienzler, 2010) See also Voltaren® Gel separate listing, where it is not recommended as a first-line treatment.

Pennsaid® (diclofenac topical solution 1.5% containing 45.5% dimethyl sulfoxide): FDA-approved for osteoarthritis of the knee. A recent study on adverse effects of this agent compared to oral diclofenac found that the latter formulation had significantly higher events. Gastrointestinal AEs orally were 39% vs. 25.4% topically ($P < 0.0001$). Cardiovascular events were 3.5% orally vs. 1.5% topically ($P = 0.055$). Liver function tests were increased more commonly in those taking oral agents. The most common adverse effect was application-site reaction. Dry skin is thought to result from the DMSO component. Long-term studies were recommended. (Roth, 2011) The dose is 40 drops to the knee four times a day. See also Pennsaid® (diclofenac sodium topical solution) separate listing, where it is not recommended as a first-line treatment.

Flector® Patch (diclofenac epolamine topical patch 1.3%): Indicated for acute strains, sprains, and contusions. Apply one patch twice daily to most painful area. See also Flector® patch (diclofenac epolamine) separate listing, where it is not recommended as a first-line treatment.

Cost effectiveness: Current FDA-approved topical agents are approximately six to ten times more expensive than oral over-the-counter preparations. Savings may occur due to lack of serious adverse GI effects, and the lack of necessity of taking an ulcer-protection medication.

Trigger points & myofascial pain: Not recommended. (Affaitati, 2009) (Dalpaiz, 2004)

Osteoarthritis of the knee: Not generally recommended unless a component of neuropathy is indicated using measures such as the Neuropathic Pain Scale. All current available studies were sponsored by the manufacturer of lidocaine patches and are non-controlled, and of short-term in duration. (Burch, 2004) (Kivitz, 2008)



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Axial back pain (including osteoarthritis): Not recommended unless neuropathy is suggested. Current studies as to use of Lidoderm patches for non-neuropathic low back pain are non-controlled, may or may not evaluate for the presence of neuropathic quality, have included multiple stages of pain (from acute to chronic), have included multiple diagnoses, show limited results in pain reduction, and are generally sponsored by the manufacturer. Acute groups have had better results than chronic pain patients, which may be attributed to natural recovery. (Gimbel, 2005) (Galer, 2004) (Argoff, 2004)

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.

Gabapentin: Not recommended. There is no peer-reviewed literature to support use.

Ketamine: Under study: Only recommended for treatment of neuropathic pain in refractory cases in which all primary and secondary treatment has been exhausted. Topical ketamine has only been studied for use in non-controlled studies for CRPS I and post-herpetic neuralgia and both have shown encouraging results. The exact mechanism of action remains undetermined.

(Gammaitoni, 2000) (Lynch, 2005)

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)**