CLEARSPRING PHARMACY™

Natural Therapies & Prescriptions That Enhance Life.™

www.clearspringrx.com

CHERRY CREEK
201 UNIVERSITY BOULEVARD, #105
DENVER, CO 80206
T 303.333.2010
F 303.333.2208

LITTLETON
8031 SOUTHPARK CIRCLE, SUITE B
LITTLETON, CO 80120
T 303.707.1500
F 303.707.1717

PCAB ACCREDITED® Compounding Pharmacy
A SERVICE OF ACHC

Customized Medications for Pain Management

Topical versus Oral NSAIDs for Acute or Chronic Pain

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed drugs worldwide and are responsible for approximately one-quarter of all reported adverse drug reactions. NSAIDs are widely prescribed for patients with rheumatic disease - a population at increased risk for serious gastrointestinal (GI) complications. Topical administration of NSAIDs offers the advantage of local, enhanced drug delivery to affected tissues with a reduced incidence of systemic adverse effects, such as peptic ulcer disease and GI hemorrhage. NSAIDs administered topically penetrate slowly and in small quantities into the systemic circulation; bioavailability and maximal plasma NSAID concentration after topical application are generally less than 5 and 15%, respectively, compared with equivalent oral administration. Topical application leads to NSAID concentrations in the muscle tissue below the site of application which are at least equivalent to that obtained with oral administration. Mason et al. conducted a systematic review and reported that topical NSAIDs were effective in relieving pain in chronic conditions like osteoarthritis and tendonitis, as well as in acute conditions like sprains and strains, with differences between individual drugs for efficacy. Rolf et al. studied the kinetics of ketoprofen in synovial fluid and intra-articular tissues in relation to plasma, and reported that topical applications of ketoprofen allow the attainment of high intra-articular tissue concentrations.

Topical NSAIDs are widely used to treat acute musculoskeletal conditions due to their potential to provide pain relief without associated systemic adverse events. Massey et al of the University of Oxford, UK, reviewed the medical databases for randomized, double-blind, active or placebo-controlled trials in which treatments were administered to adult patients with acute pain resulting from strains, sprains or sports or overuse-type injuries (twisted ankle, for instance). Forty-seven studies were included in a meta-analysis; most compared topical NSAIDs in the form of a gel, spray, or cream with a similar placebo, with 3455 participants in the overall analysis of efficacy. Clinical success was defined as 50% pain relief. For treatment periods of 6 to 14 days, topical diclofenac, ibuprofen, ketoprofen, and piroxicam were of similar efficacy, but indomethacin and benzydamine were not significantly better than placebo. Local skin reactions were generally mild and transient, and did not differ from placebo. There were very few systemic adverse events or withdrawals due to adverse events. The analysis concluded: "Topical NSAIDs can provide good levels of pain relief, without the systemic adverse events associated with oral NSAIDs, when used to treat acute musculoskeletal conditions."

Regarding chronic pain, a review of 14 double blind placebo-controlled trials with information from almost 1,500 patients showed that topical NSAIDs were significantly more effective than placebo. Results were not affected by trial quality, validity or size, outcome reported, or condition treated. Local adverse events (6%), systemic adverse events (3%), or the numbers withdrawing due to an adverse event were the same for topical NSAID and placebo. Topical NSAIDs were effective and safe in treating chronic musculoskeletal conditions for two weeks (duration studied). Three trials with 764 patients comparing a topical with an oral NSAID found no difference in efficacy.

Topically applied NSAIDs have a superior safety profile to oral formulations. Adverse effects secondary to topical NSAID application occur in approximately 10 to 15% of patients and are primarily cutaneous in nature (rash and pruritus

at site of application). GI adverse drug reactions are rare with topically applied NSAIDs, compared with a 15% incidence reported for oral NSAIDs.

Cochrane Database Syst Rev. 2010 Jun 16;6:CD007402.
BMC Musculoskelet Disord 2004 Aug 19;5:28
Drugs 2000 Sep;60(3):555-74
Rheumatology (Oxford) 1999 Jun;38(6):564-7

Sample Prescription

Compounded Medication

Ketoprofen 20% in Lipoderm
Sig: Apply 1 cc (pea-size amount) QID to relieve pain and inflammation.
Disp: 60 gm.

NMDA Receptor Antagonists for Management of Pain

Dextromethorphan (DM) is a noncompetitive NMDA receptor antagonist, which is widely used as an antitussive agent. DM also prevents neuronal damage and modulates pain sensation via noncompetitive antagonism of excitatory amino acids (EAAs). DM has been found to be useful in the treatment of pain in cancer patients, the treatment of methotrexate-induced neurotoxicity, and as an adjunct to routine postoperative pain management.

CNS Drug Rev. 2007 Spring;13(1):96-106.
Curr Opin Anaesthesiol. 2009 Oct;22(5):618-22.

Custom doses of dextromethorphan are available by prescription from Clear Spring Pharmacy.

Neuropathic Pain Syndromes

Neuropathic pain occurs in a significant portion of cancer patients and can present as a diverse set of syndromes. Changes may occur in the peripheral, central and autonomic nervous system and each can contribute to the development of chronic neuropathic pain. Cancer patients with neuropathic pain report symptoms of paresthesias and dysesthesias, as well as allodynia, and hyperalgesia. Multiple neuropathic cancer pain syndromes are caused by direct infiltration of the tumor, including cranial nerve neuralgias, mononeuropathies, radiculopathies, plexopathies (cervical, brachial and lumbosucral), as well as central pain from spinal cord compression. Chemotherapeutic agents can cause neuropathic pain and radiation therapy may also induce injury, leading to microvascular insufficiency and fibrotic changes affecting the nerves and perineural tissues. Surgery for diagnostic or therapeutic purposes may lead to chronic neuropathic pain. Other conditions, such as herpes zoster, may also produce neuropathic pain in cancer patients.

Combinations of various classes of medications are often effective in treating neuropathic pain. Topically applied drugs are absorbed systemically only in minute quantities, so systemic side effects and pharmacological interactions with systematic medications are usually negligible. Our compounding pharmacist will work together with physicians and patients to customize a preparation containing the most appropriate medications for each patient.

Sample Prescription

Compounded Medication

Gabapentin 6% / Clonidine 0.2% / Lidocaine HCl 2% / Ketamine 10% in Lipoderm
Sig: Apply 1 cc (pea-size amount) QID to relieve pain.
Disp: 60 gm.

Topical Treatment for Chemotherapy-Induced Peripheral Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a troublesome chronic symptom that has no proven pharmacologic treatment. Barton et al. of the Mayo Clinic College of Medicine conducted a double-blind randomized placebo-controlled trial to evaluate a novel compounded topical gel. Patients (n=208) with CIPN were randomized to receive topical baclofen 10 mg, amitriptyline HCL 40 mg, and ketamine 20 mg in a pluronic lecithin organogel (BAK-PLO) or placebo (PLO) to determine its effect on numbness, tingling, pain, and function. The primary endpoint was the baseline-adjusted sensory subscale of the EORTC QLQ-CIPN20, at 4 weeks.

Patients who received BAK-PLO experienced greater improvement in both sensory and motor subscales. The greatest improvements were related to the symptoms of tingling, cramping, and shooting/burning pain in the hands as well as difficulty in holding a pen. There were no undesirable toxicities associated with the BAK-PLO and no evidence of systemic toxicity. The research concluded that further research is needed with increased doses to better clarify the clinical role of this treatment in CIPN.

Support Care Cancer. 2011 Jun;19(6):833-41.

Ask us about other customized medications and special bases for treatment for neuropathic pain. Clear Spring Pharmacy can expand the practitioner's armamentarium by formulating therapies that meet the specific needs of each patient.

Sample Prescription

Compounded Medication

Baclofen 5% / Amitriptyline HCl 2% / Ketamine HCl 5% in Lipoderm
Sig: Apply 1 cc (pea-size amount) QID to relieve pain.
Disp: 60 gm.