EUROPEAN AUTHORITIES RECOMMEND APPROVAL FOR IONSYS

IONSYS, a transdermal fentanyl delivery system produced by the ALZA Corporation (Mountain View, CA), has been recommended for approval in Europe. The system is approximately the size of a credit card, and can be attached to a patient's upper arm or chest. Patients can push a button to receive a small dose of fentanyl, a short-acting prescription opioid analgesic.

The manufacturer of IONSYS claims that through the use of the E-TRANS drug delivery system (also found in ALZA's Duragesic transdermal fentanyl patches), the drug is transported through intact skin via low-level electrical energy, providing a rapid onset of action and sustained effect comparable to that seen with intravenous dosing. In addition, IONSYS dosing can be easily adjusted incrementally to suit patient-specific needs.

Once formal approval has been received, Janssen-Cilag will market the system throughout Europe. In the United States, IONSYS is currently under review by the Food and Drug Administration. Ortho-McNeil will market the product if approval is received. (Source: Drug Policy Central Web site, October 17, 2005.)

OPIOID USE AND NSAIDS IN MIGRAINES

A recent study headed by Dr. Rami Burstein, an Associate Professor at Harvard Medical School and Vice Chairman of Research of the Department of Anesthesia and Critical Care at Beth Israel Deaconess Medical Center, found that patients with a history of opioid use received no benefit from intravenous nonsteroidal anti-inflammatory drugs (NSAIDs) during treatment for migraine headaches. The study consisted of 32 participants with advanced migraines whom had developed allodynia (skin hypersensitivity).

One-half of the study participants received the NSAID ketorolac (Toradol, Roche Laboratories, Inc., Nutley, NJ) delivered intravenously beginning four hours after the start of a migraine. The other participants received an injection of one of the triptans (sumatriptan) four hours after the migraine began, followed by ketorolac two hours later, if the pain had not subsided. With the ketorolac infusion, 64 percent of the patients were pain-free one hour after, with skin sensitivity returning to normal. However, 32 percent received no benefit at all, and it was noted that these individuals all had a previous history of using opioids.

According to Dr. Burstein, NSAIDs were chosen for this study because previous research had shown that inflammatory molecules play a role in chronic pain, including frequent migraines. These inflammatory molecules are found in the periphery of the body and also the central nervous system. Whereas NSAIDs in pill form block inflammation only in the periphery, they can reach high enough concentrations to block inflammatory production in the central nervous system in intravenous form.

Previous research has indicated that once allodynia occurs, triptans—drugs commonly used to treat migraines—no longer work. Once this occurs, migraine patients visiting the emergency room often are given an infusion of opioids (51 percent, according to one 1998 survey). With the results of this new study, Dr. Burstein recommends that physicians revisit the prescription of opioids for migraine patients and consider intravenous NSAIDs as a viable, nonhabit-forming alternative. (Source: *Times Herald-Record* Web site, October 19, 2005.)

PHASE II TRIAL FOR ABUSE-RESISTANT EXTENDED-RELEASE OPIOID

Alpharma, Inc. has received clearance from the US Food and Drug Administration to begin a Phase II trial of an abuse-resistant extended-release opioid. Target audiences for the product include individuals with chronic moderate to severe cancer- and noncancer-related pain. Alpharma also currently produces Kadian, a sustained-release morphine product.

The new product features a combination of an extended-release opioid with an antagonist in a single tablet. Tampering with the dose (e.g., crushing, chewing, or dissolving the tablet) will cause the antagonist to be released, thereby suppressing the opioid's effects. Alpharma hopes that this product will help improve the treatment of patients with chronic pain and also reduce the potential for abuse of opioid medications by eliminating the ability of patients to use the medication in any way other than that intended by the prescribing physician. (Source: Alpharma, Inc. press release, October 10, 2005.)

μ-OPIOID THERAPY AND CHRONIC ARTHRITIS PAIN

Led by Dr. Jason McDougall, researchers at the University of Calgary recently conducted an experiment on the effectiveness of endomorphin 1, a natural morphinelike

compound, in lieu of morphine in knee joint pain. Male rats with induced acute and chronic arthritis were used in the study, in which endomorphin 1 was injected into affected knee joints. The effectiveness was measured by joint edema formation and sensory nerve activity associated with pain.

The rats with acute arthritis showed a reduction in joint nerve hypersensitivity of up to 75 percent. However, the rats with chronic arthritis showed no observable effect on the telltale triggers of pain. From these results, Dr. McDougall and colleagues concluded that chronic inflammation negates the pain-relieving benefits of the body's μ-opioid receptors, and that the endogenous opioid system may be inadequate in alleviating chronic arthritis pain.

Details of the study appear in the October 2005 issue of *Arthritis & Rheumatism*, which is available online at *http://interscience.wiley.com/journal/arthritis*. (Source: Medical News Today, October 1, 2005.)

REDUCED OPIOID AVAILABILITY IN MINORITY AREAS

Pharmacies in minority neighborhoods are much less likely to carry sufficient supplies of frequently prescribed opioid medications than those in white neighborhoods, as reported in a study led by Dr. Carmen R. Green of the University of Michigan Medical School. In this study, it was found that pharmacies in wealthy black neighborhoods were no more likely to carry opioids than those in poorer black neighborhoods; however, pharmacies in wealthy white neighborhoods were far more likely to carry opioids than those in poorer white neighborhoods. In addition, 91 percent of independent pharmacists were found to have adequate stock, whereas only 59 percent of chain stores met the criteria.

The study surveyed 188 Michigan pharmacies. Of those pharmacies, 87 percent within predominantly white Zip codes were found to have sufficient supplies of opioids, compared to only 54 percent in predominantly minority Zip codes. Dr. Green and other researchers noted that their study is consistent with earlier ones that showed doctor reluctance in prescribing opioids to minority patients.

One possible nonclinical explanation for lower availability offered by the authors is concern over potential illicit use and ensuing consequences for the dispenser. Several of the surveyed pharmacists echoed that concern, as did Susan Winkler, the Vice President for Policy of the American Pharmaceutical Association. Winkler also noted that pharmacists carry the burden of determining whether prescriptions are actually valid and/or clinically appropriate, with heavy fines as a consequence and limiting factor in the decision to stock medications with high potential for abuse.

In response to the study results concerning chain stores, Valerie Stork, spokeswoman for the National Association of Chain Drug Stores, stated that although the Drug Enforcement Administration tracks and monitors the sale of controlled drugs, there is no direct mandate on how much of a medication each pharmacy must carry.

The study appears in the October 2005 issue of the *Journal of Pain*. (Source: *The Washington Post* Web site, October 15, 2005.)