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Statement prepared for: Anesthetic and Life Support Drugs Advisory Committee, FDA
September 13-14, 2001

Submitted by: Glenda Dahlquist, MD
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Specialty: Chronic Pain Management

Board certifications: American Board of Anesthesiology (1993)
American Board of Pain Medicine (1997)
American Board of Anesthesiology/Pain Management (1998)

Topic: Modified-release Opioid Analgesics in the Treatment of Patients with Chronic Pain of Non-malignant Etiology

Adequate and effective treatment of pain in the United States remains a major problem. Even recent studies show that approximately 50 percent of hospitalized patients surveyed describe their pain as inadequately controlled. It is felt that inadequacy of pain management is in large part due to physician fears of regulatory sanctions when prescribing strong pain killers (such as opioid analgesics,) as well as fears of creating addiction in the patients treated with opioid analgesics. Unfortunately, in many cases of severe chronic pain, opioid analgesics are the only medication which will provide enough relief of pain for the patient to be able to function with a reasonably normal life-style and enjoy a quality of life without constant misery.

Thanks to research of Dr. Russell Portenoy, Dr. David Haddox (past President of the American Academy of Pain Medicine,) and many others, it has been shown consistently in the past decade that patients with chronic non-malignant pain treated with opioids generally do not develop addiction to the opioid medication given. An excellent review article by Russell Portenoy, MD, published in the Journal of Pain And Symptom

Management, vol. 11, no. 4, pp. 203-217, Opioid Therapy for Chronic Nonmalignant Pain: A Review of the Critical Issues, addresses this in great detail. In many studies, the percentage developing iatrogenic addiction to the opioid medication has been less than 1-2 percent.

If one examines studies of addition, most studies will show that approximately 3-17 percent of the general population is addicted to some substance. (This includes all substances of abuse; not just opioid.) If these statistics are applied to the chronic pain patients population, one may deduce that 3-17 percent of this sub-population will also have issues of substance addiction (again addition to some substance; not necessarily to opioids.)

According to new research presented at the annual meeting of the American Academy of Pain Medicine in February, 2001, the best predictors of whether or not a patient will become iatrogenically addicted to an opioid analgesic prescribed for chronic non-malignant pain were: 1) History of polysubstance abuse (abuse of 3 or more different substances); 2) Admitted previous addiction to opioid medications; or 3) Previous participation in a drug rehabilitation facility. In this study, it was noted that a person with previous history of addiction to only one or two substances other than opioids had no higher development of iatrogenic addition to prescribed opioids for chronic nonmalignant pain than did people with no history of addiction to any substance. Given these data, it is easy to see why earlier studies showed iatrogenic development of addiction specifically to prescribed opioids for chronic pain to be so low (less than 1-2 percent.)

Given the effectiveness of opioids in chronic pain management, and given the low incidence of development of iatrogenic addiction with these medications, the American Academy of Pain Medicine, in conjunction with the American Pain Society, in 1997 issued a joint position paper outlining guidelines for physicians to safely prescribe opioids and monitor those patients for whom the opioids had been prescribed. Shortly thereafter, using these guidelines, the national Federation of State Medical Boards made recommendations for individual state medical boards to adopt similar guidelines in order to protect physicians from unwarranted sanctions in prescribing of controlled substances for chronic non-malignant pain. To date, the vast majority of state medical boards have adopted these guidelines.

Despite the fact that physicians are now protected from regulatory sanctions against their medical licenses (provided that they follow recommended guidelines for prescribing controlled substances for chronic non-malignant pain,) and despite the fact that it has been shown that less than 1-2 percent of patients receiving opioid medications for chronic non-malignant pain will develop an iatrogenic addiction to the medication, inadequate treatment of pain still exists in dramatically high proportions.

So, why is this?

Recently, much publicity had been focused on the abuse and illicit use of opioids, specifically the modified release opioids. This type of abuse is generally related to using the medication via routes of administration not recommended by the way the medication has been prescribed. Most common misuses of these medications include chewing the pills before swallowing, crushing the medication, snorting the medication, and/or intravenously injecting the medication, when the medication is intended only for swallowing the pill intact and in the quantities prescribed by the physician. When taken properly, these modified release opioids will not produce a rapid rise in serum levels of the drug. Therefore, if used properly, they present little addictive potential, since one of the prerequisites for addictive potential is rapid release of a centrally acting substance into the circulation leading to rapid rise in the brain. Medications with slow rise in serum levels do not produce the "high" feeling that addicts seek.

One of the major pharmaceutical companies is currently doing studies to combine Naltrexone, an opioid antagonist (or reversal agent) in a matrix designed to slowly release the opioid. With this type of matrix, if the medication is swallowed and digested, the opioid will be released slowly into the bloodstream, while the Naltrexone will be maintained within the matrix unabsorbed, so as not to negate the pain-relieving effects of the opioid. However, if the medication matrix is destroyed either physically by crushing or chemically by dissolving the matrix, the Naltrexone will be released, blocking the action of the opioid in the brain. Thus, if taken improperly via routes mentioned above, the modified release opioids, if manufactured in this manner, will no longer retain their street value and potential for abuse/misuse. This should be available within the next few years.

In the meantime, limiting use of prescription opioids for treatment in patients suffering from severe, unrelenting, non-malignant pain would only aggravate a situation which was just beginning to be corrected by action of the national Federal of State Medical Boards and availability of current pain management research. If left with inadequate treatment, many of these patients will be forced out of work and onto disability, draining federal and state governments of billions of dollars. Untreated or inadequately treated pain, one of the major causes of depression and suicide, will dramatically rise. I ask you, are deaths due to suicide any less of a concern than deaths due to misuse of medications?

This does not even account for the fact that untreated/inadequately treated pain will lead to other sequelae of illnesses such as hypertension, increase in heart disease and other chronic illness due to chronic elevations of stress hormones and inhibition of properly functioning immune systems. These conditions are already well-known causes for premature deaths and morbidity.

One must also consider that patients with inadequately treated pain often turn to over-the-counter non-steroidal anti-inflammatory agents to treat their pain. Those with severe pain will frequently use these medications in quantities well above the recommended dosages.

Overdosages due to misuse of non-steroidal anti-inflammatory medications can lead to fatal GI bleeds and renal failure, not to mention liver failure; all very significant health problems.

Finally, those with inadequately treated pain will often become so aggravated with the situation that they will turn to other mind-altering substances of abuse (such as alcohol, marijuana, or diverted opioids) to dull their own perception of their unrelenting pain and suffering. So, in several cases, limiting opioid availability for proper treatment of pain may actually lead to abuse of and addictions to other substances.

Physicians who are properly trained in pain management are becoming increasingly more aware and savvy when it comes to recognizing addictive and medication abuse patterns in patients. Most have policies in place to deal with situations of misuse/abuse of medication as soon as the problem becomes suspect in a patient. Communication is continuing to improve among treating physicians, pharmacists, other health care workers, and local law-enforcement agencies which should help to decrease the abuse/misuse of opioid analgesics now and in the future.

I urge you to carefully evaluate all these facts when considering the limitation of opioid analgesics for chronic non-malignant pain management. As a chronic pain management physician who is intimately involved with people who come to me with inadequately treated pain on a regular basis, I believe that the consequences of limiting proper use of opioids for this prevalent condition will be much grater than the prevalence of consequences due to misuse of modified release opioid medications is today, if prescribing of these medications is limited. Therefore, I recommend that availability of pharmaceutically-produced modified release opioid analgesic not be restricted beyond the medical need for these medications.

I would appreciate the opportunity to voice my opinion on these issues at your Anesthetic and Life Support Drugs Advisory Committee meeting to be held on September 13-14, 2001. Please contact me at the above address (or phone number) if it will be possible for me to speak to your committee. Thank you.

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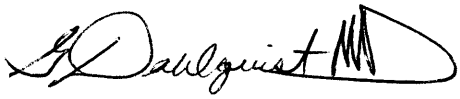

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