American Society of Anesthesiologists

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August 22, 2012

Margaret Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993

Dear Commissioner Hamburg:

The American Society of Anesthesiologists (ASA), on behalf of over 48,000 members, is writing in response to the petition to change the label of opioid analgesics submitted by Physicians for Responsible Opioid Prescribing (PROP). The petition requests that the Food and Drug Administration (FDA):

1) Strike the term "moderate" from the indication for non-cancer pain.
2) Add a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain.
3) Add a maximum duration of 90-days for continuous (daily) use for non-cancer pain.

As the medical specialty representing the largest number of practicing pain medicine physicians and the recognized leaders in patient safety, ASA has significant interest in reducing the misuse, abuse, and diversion of opioid medications that have led to unintended deaths. We support the broad concept that high dose opioids should not be used to treat chronic non-cancer pain. However, placing specific limits on daily doses of opioids that a physician may prescribe is not scientifically founded nor is it practical.

A fundamental flaw shared by all three components of the PROP proposal is the intrinsic difficulty in defining "non-cancer pain." Improvements in cancer therapy have resulted in increases in survival duration as well as cure rates, although the treatments used to achieve these beneficial results often themselves lead to chronic pain. Who will decide whether the persistent pain, for example, of nerve damage incurred during an otherwise curative course of chemo- and radiation therapy is or is not cancer-related?

With regard to the first proposed change, it is very common for pain intensity to fluctuate during long-term treatment of chronic non-cancer pain. Pain that is moderate at one time may be severe a few hours later, then decline to become moderate shortly after. Pain that is moderate at rest typically increases to severe when the patient undertakes desirable physical activity. Hence, patients are often instructed to self-medicate with an opioid shortly before anticipated physical activity in order to keep it from becoming severe. It would not be practical to instruct patients never to take an opioid during intervals when their pain is moderate, but only to do so when their pain is severe.

With regard to the second proposal, considerable clinical experience attests to substantial interindividual differences in the analgesic effect of morphine and other opioids. The population-based conversion factors used to calculate "equivalent" morphine doses in patients treated with non-morphine opioids differ from patient to patient, and even in the same patient followed across time (e.g., with declining kidney or liver function, or dehydration).

With regard to the third proposal, opioids for moderate pain, high dose opioids, or opioids taken for longer than 90 days may be effective for certain patients and should continue to be a treatment option if clinically appropriate. The petitioners set strict limits on dose and duration of opioid therapy for non-cancer pain based upon group statistics. However, just as it is illogical to generalize observations from a single patient to guide the treatment of an entire group of patients, the converse is also true. One cannot use population-based, aggregate epidemiological findings to set specific limits that are valid for every patient, given the interindividual differences in pathophysiology and opioid responsiveness of seemingly identical chronic non-cancer pain conditions.

ASA advocates for an approach more flexible than the strict limits requested in the petition. The petitioners use epidemiologic data to draw conclusions as to dosage and duration that would more appropriately be presented as guidelines, not mandates, for the treatment of large unselected populations such as are seen in primary care. Pain treatment physicians see complex patients who by definition are selected outliers whose problems have persisted or worsened during nonspecialist care. Mandating rigid, across-the-board limits on opioid dosage and duration would add difficulty to our already-challenging task of caring for this subgroup of outlier patients.

ASA strongly believes that access to opioids must be balanced with efforts to reduce the misuse, abuse, and diversion of these medications. Federal and state governments, health care professionals, law enforcement, and other stakeholders are implementing initiatives to curb prescription drug abuse while maintaining patient access to the medications they need. ASA has had the pleasure to work with stakeholders on these initiatives, which include health care professional education, prescription drug monitoring, and medication storage and disposal.

Further, we agree with many in the pain treatment community that additional research should be conducted on the long-term efficacy of opioids for chronic pain. Fundamental questions bearing upon the benefit-to-risk ratio of opioids and other treatments for chronic non-cancer pain must be resolved, such as the percentages of patients of various ages and genders who will become tolerant, dependent upon, or addicted to opioids during long-term therapy. This effort must be accomplished in a comprehensive fashion, accommodating individual variability and the diversity of our nation's population, and supplementing results from randomized controlled trials with outcomes data on treatment effectiveness in everyday settings of care. We understand that such studies are now being planned with FDA support, as their results will provide a scientific basis to inform public policy and regulatory actions.

We look forward to continue working with the FDA on this important issue. Please feel free to contact Lisa Pearlstein, J.D., Pain Medicine and Regulatory Lobbyist at l.pearlstein@asawash.org or 202-289-2222 if you have any questions or need additional information regarding this issue.

Sincerely,

Jerry A. Cohen, M.D.
President
American Society of Anesthesiologists

cc: Bob Rappaport, M.D.